Treatment of Depression During Pregnancy and the Postpartum Period

Appendixes

Appendix A. Search Strategies

CINAHL Plus with Full Text 1941-December 2012
S1 MH Pregnancy+
S2 "pregnan*"
S3 MH Postnatal Period+
S4 (MH "Affective Disorders+")
S5 MH Seasonal Affective Disorder
S6 MH Depression+ OR MH Depression, Postpartum
S7 MH Serotonin Uptake Inhibitors+
S8 "selective serotonin reuptake inhibitor"
S9 "ssri"
S10 MH Citalopram OR citalopram
S11 "escitalopram"
S12 MH Fluoxetine OR fluoxetine OR MH Olanzapine-Fluoxetine
S13 MH Fluvoxamine Maleate OR fluvoxamine
S14 MH Sertraline Hydrochloride OR sertraline
S15 MH Paroxetine OR paroxetine
S16 "celexa"
S17 "lexapro"
S18 "prozac"
S19 "luvox"
S20 "zoloft"
S21 "paxil"
S22 MH Desvenlafaxine Succinate OR desvenlafaxine
S23 MH Mirtazapine OR mirtazapine
S24 "pristiq"
S25 MH Venlafaxine OR effexor
S26 "noradrenergic and specific serotonergic reuptake inhibitor"
S27 (MH "Duloxetine Hydrochloride") OR "duloxetine"
S28 "cymbalta"
S29 (MH "Norepinephrine") OR "norepinephrine"
S30 MH Dopamine Uptake Inhibitors OR dopamine reuptake inhibitor
S31 MH Bupropion OR bupropion
S32 "wellbutrin"
S33 MH Nefazodone OR nefazodone
S34 "serzone"
S35 (MH "Antidepressive Agents+") OR (MH "Antidepressive Agents, Tricyclic+")
S36 (MH "Amitriptyline") OR "amitriptyline"
S37 (MH "Imipramine") OR "imipramine"
S38 (MH "Desipramine") OR "desipramine"
S39 (MH "Nortriptyline") OR "nortriptyline"
S40 MH Teratogens OR teratogenicity
S41 S1 OR S2 OR S3
S42 S4 OR S5 OR S6

S43 S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39
S44 S41 AND S42 AND S43
S45 S40 AND S43
S46 S44 OR S45
S47 S44 OR S45

EBM Reviews - Cochrane Central Register of Controlled Trials December 2012
1 exp Pregnancy/
2 pregnan$.mp.
3 Perinatal Care/
4 Postnatal Care/
5 Peripartum Period/
6 exp Postpartum Period/
7 mood disorders/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/
8 Depression/
9 (depressi$ or dysthymi$ or "mood disorder$" or "seasonal affective disorder" or sad).mp.
10 or/7-9
11 10 and (de or dh or dt or pc or th).fs.
12 Serotonin Uptake Inhibitors/
13 (selective serotonin reuptake inhibitor$ or ssri).mp.
14 (citalopram or escitalopram or fluoxetine or fluvoxamine or sertraline or paroxetine).mp.
15 (celexa or lexapro or prozac or luvox or zoloft or paxil).mp.
16 serotonin norepinephrine reuptake inhibitor.mp.
17 (desvenlafaxine or mirtazapine).mp.
18 (pristiq or effexor).mp.
19 (noradrenergic and specific serotonergic reuptake inhibitor).mp.
20 remeron.mp.
21 (selective serotonin and norepinephrine reuptake inhibitor).mp.
22 ssnri.mp.
23 (duloxetine or cymbalta).mp.
24 (norepinephrine and dopamine reuptake inhibitor).mp.
25 ndri.mp.
26 (bupropion or wellbutrin).mp.
27 (nefazodone or serzone).mp.
28 (olanzapine adj1 fluoxetine).mp.
29 exp Antidepressive Agents/
30 Antidepressive Agents, Tricyclic/
31 (amitriptyline or imipramine).mp.
32 desipramine.mp. or Desipramine/
33 nortriptyline.mp. or Nortriptyline/
34 or/12-33
35 exp Prenatal Injuries/

36 exp Maternal Exposure/
37 exp Pregnancy Complications/
38 exp Pregnancy Outcome/
39 exp Fetal Development/
40 or/35-39
41 exp Infant/
42 exp Infant Mortality/
43 exp child/ or exp child, preschool/
44 (infant$ or child$ or pediatri$).mp.
45 or/41-44
46 exp Prenatal Care/
47 exp Preconception Care/
48 Abnormalities, Drug-Induced/ or Prenatal Exposure Delayed Effects/
49 teratogen$.mp.
50 or/1-6
51 (pregnan$ or perinatal or postpartum).mp.
52 50 or 51
53 46 or 47 or 52
54 48 or 49
55 11 and 34 and 53
56 34 and 40
57 34 and 54
58 34 and 45 and 52
59 or/55-58

EBM Reviews - Cochrane Database of Systematic Reviews 2005 to November 2012
1. (depressi$ or bipolar$ or dysthymi$ or cyclotymi$ or "mood disorder$" or "seasonal affective disorder" or sad).mp.
2. (selective serotonin reuptake inhibitor$ or ssri).mp.
3. (citalopram or escitalopram or fluoxetine or fluvoxamine or sertraline or paroxetine).mp.
4. (celexa or lexapro or prozac or luvox or zoloft or paxil).mp.
5. serotonin norepinephrine reuptake inhibitor.mp.
6. (desvenlafaxine or mirtazapine).mp.
7. (pristiq or effexor).mp.
8. (noradrenergic and specific serotonergic reuptake inhibitor).mp.
9. mirtazapine.mp.
10. remeron.mp.
11. (selective serotonin and norepinephrine reuptake inhibitor).mp.
12. ssnri.mp.
13. (duloxetine or cymbalta).mp.
14. (norepinephrine and dopamine reuptake inhibitor).mp.
15. ndri.mp.
16. (bupropion or wellbutrin).mp.
17. (nefazodone or serzone).mp.
18. (olanzapine adj1 fluoxetine).mp.

19. antidepressant$.mp.
20. (amitriptyline or imipramine or desipramine or nortriptyline).mp.
21. (pregnan$ or prenatal$ or postnatal$ or peripartum or postpartum).mp.
22. or/2-20
23. 1 and 21 and 22
24. limit 23 to full systematic reviews

Ovid MEDLINE and Ovid OLDMEDLINE 1946 to November Week 3 2012

1. exp Pregnancy/
2. pregnan$.mp.
3. Perinatal Care/
4. Postnatal Care/
5. Peripartum Period/
6. exp Postpartum Period/
7. mood disorders/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/
8. Depression/
9. (depressi$ or dysthymi$ or "mood disorder$" or "seasonal affective disorder" or sad).mp.
10. or/7-9
11. 10 and (de or dh or dt or pc or th).fs.
12. Serotonin Uptake Inhibitors/
13. (selective serotonin reuptake inhibitor$ or ssri).mp.
14. (citalopram or escitalopram or fluoxetine or fluvoxamine or sertraline or paroxetine).mp.
15. (celexa or lexapro or prozac or luvox or zoloft or paxil).mp.
16. serotonin norepinephrine reuptake inhibitor.mp.
17. (desvenlafaxine or mirtazapine).mp.
18. (pristiq or effexor).mp.
19. (noradrenergic and specific serotonergic reuptake inhibitor).mp.
20. remeron.mp.
21. (selective serotonin and norepinephrine reuptake inhibitor).mp.
22. ssnri.mp.
23. (duloxetine or cymbalta).mp.
24. (norepinephrine and dopamine reuptake inhibitor).mp.
25. ndri.mp.
26. (bupropion or wellbutrin).mp.
27. (nefazodone or serzone).mp.
28. (olanzapine adj1 fluoxetine).mp.
29. exp Antidepressive Agents/
30. Antidepressive Agents, Tricyclic/
31. (amitriptyline or imipramine).mp.
32. desipramine.mp. or Desipramine/
33. nortriptyline.mp. or Nortriptyline/
34. or/12-33
35. exp Prenatal Injuries/
36. exp Maternal Exposure/

37. exp Pregnancy Complications/
38. exp Pregnancy Outcome/
39. exp Fetal Development/
40. or/35-39
41. exp Infant/
42. exp Infant Mortality/
43. exp child/ or exp child, preschool/
44. (infant$ or child$ or pediatri$).mp.
45. or/41-44
46. exp Prenatal Care/
47. exp Preconception Care/
48. Abnormalities, Drug-Induced/ or Prenatal Exposure Delayed Effects/
49. teratogen$.mp.
50. or/1-6
51. (pregnan$ or perinatal or postpartum).mp.
52. 50 or 51
53. 46 or 47 or 52
54. 48 or 49
55. 11 and 34 and 53
56. 34 and 40
57. 34 and 54
58. 34 and 45 and 52
59. or/55-58
60. limit 59 to humans
61. limit 60 to english language
62. limit 60 to abstracts
63. 61 or 62

PsychInfo 1806 to December Week 2 2012
1. exp Pregnancy/
2. pregnan$.mp.
3. mood disorders/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or seasonal affective disorder/
4. Depression/
5. (depressi$ or dysthymi$ or "mood disorder$" or "seasonal affective disorder" or sad).mp.
6. (selective serotonin reuptake inhibitor$ or ssri).mp.
7. (citalopram or escitalopram or fluoxetine or fluvoxamine or sertraline or paroxetine).mp.
8. (celexa or lexapro or prozac or luvox or zoloft or paxil).mp.
9. serotonin norepinephrine reuptake inhibitor.mp.
10. (desvenlafaxine or mirtazapine).mp.
11. (pristiq or effexor).mp.
12. (noradrenergic and specific serotonergic reuptake inhibitor).mp.
13. mirtazapine.mp.
14. remeron.mp.

15. (selective serotonin and norepinephrine reuptake inhibitor).mp.
16. ssnri.mp.
17. (duloxetine or cymbalta).mp.
18. (norepinephrine and dopamine reuptake inhibitor).mp.
19. ndri.mp.
20. (bupropion or wellbutrin).mp.
21. (nefazodone or serzone).mp.
22. (olanzapine adj1 fluoxetine).mp.
23. (amitriptyline or imipramine or desipramine or nortriptyline).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
24. exp Tricyclic Antidepressant Drugs/ or exp Antidepressant Drugs/
25. exp Pregnancy Outcome/
26. (infant$ or child$ or pediatri$).mp.
27. 1 or 2
28. or/3-5
29. or/6-24
30. 25 and 26
31. 27 and 28 and 29
32. 29 and 30
33. 31 or 32

Sciverse Scopus 1974 to December 2012
(TITLE-ABS-KEY((pregnan*) AND ("mood disorder*" OR "affective disorder*" OR "depressive disorder" OR depression OR "seasonal affective disorder" OR "dysthymic disorder")) OR (TITLE-ABS-KEY(teratogen*)) AND ((TITLE-ABS-KEY(antidepressant* OR antidepressive agent* OR "selective serotonin reuptake inhibitor*" OR "ssri" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR sertraline OR paroxetine OR celexa OR lexapro OR prozac OR luvox OR zoloft OR paxil OR desvenlafaxine OR mirtazapine OR pristiq OR effexor OR “noradrenergic and specific serotonergic reuptake inhibitor" OR "selective serotonin and norepinephrine reuptake inhibitor" OR "ssnri" OR "norepinephrine and dopamine reuptake inhibitor" OR bupropion OR wellbutrin OR nefazodone OR serzone OR amitriptyline OR imipramine OR desipramine OR nortriptyline OR remeron OR olanzapine))

Appendix B. Included Studies

Observational studies

1. Alwan S, Reefhuis J, Botto LD, et al. Maternal use of bupropion and risk for congenital heart defects. American Journal of Obstetrics & Gynecology. 2010 Jul;203(1):52.e1-6. PMID: 20417496.

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7. Bérard A, Ramos É, Rey É, et al. First trimester exposure to paroxetine and risk of cardiac malformations in infants: The importance of dosage. Birth Defects Research Part B - Developmental and Reproductive Toxicology. 2007;80(1):18-27.

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11. Bracken MB, Holford TR. Exposure to prescribed drugs in pregnancy and association with congenital malformations. Obstetrics and Gynecology. 1981;58(3):336-44.

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14. Chambers CD, Johnson KA, Dick LM, et al. Birth outcomes in pregnant women taking fluoxetine. New England Journal of Medicine. 1996 Oct 3;335(14):1010-5. PMID: 8793924.

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16. Cole JA, Ephross SA, Cosmatos IS, et al. Paroxetine in the first trimester and the prevalence of congenital malformations. Pharmacoepidemiology & Drug Safety. 2007 Oct;16(10):1075-85. PMID: 17729379.

17. Cole JA, Modell JG, Haight BR, et al. Bupropion in pregnancy and the prevalence of congenital malformations. Pharmacoepidemiology & Drug Safety. 2007 May;16(5):474-84. PMID: 16897811.

18. Colvin L, Slack-Smith L, Stanley FJ, et al. Linking a pharmaceutical claims database with a birth defects registry to investigate birth defect rates of suspected teratogens. Pharmacoepidemiology and Drug Safety. 2010;19(11):1137-50.

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30. Einarson A, Bonari L, Voyer-Lavigne S, et al. A multicentre prospective controlled study to determine the safety of trazodone and nefazodone use during pregnancy. Canadian Journal of Psychiatry. 2003;48(2):106-10.

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32. Einarson A, Choi J, Einarson TR, et al. Incidence of major malformations in infants following antidepressant exposure in pregnancy: results of a large prospective cohort study. Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie. 2009 Apr;54(4):242-6. PMID: 19321030.

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35. El Marroun H, Jaddoe VWV, Hudziak JJ, et al. Maternal use of selective serotonin reuptake inhibitors, fetal growth, and risk of adverse birth outcomes. Archives of General Psychiatry. 2012 Jul;69(7):706-14. PMID: 22393202.

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Randomized Controlled Trials

1. Appleby L, Warner R, Whitton A, et al. A controlled study of fluoxetine and cognitive-behavioural counselling in the treatment of postnatal depression. BMJ. 1997 Mar 29;314(7085):932-6. PMID: 9099116.

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4. Logsdon MC, Wisner K, Hanusa BH. Does maternal role functioning improve with antidepressant treatment in women with postpartum depression? Journal of Women's Health. 2009 Jan-Feb;18(1):85-90. PMID: 19132881.

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8. Wan MW, Sharp DJ, Howard LM, et al. Attitudes and adjustment to the parental role in mothers following treatment for postnatal depression. Journal of Affective Disorders. 2011 Jun;131(1-3):284-92. PMID: 21349585.

9. Wisner KL, Hanusa BH, Perel JM, et al. Postpartum depression: a randomized trial of sertraline versus nortriptyline. Journal of Clinical Psychopharmacology. 2006 Aug;26(4):353-60. PMID: 16855451.

10. Yonkers KA, Lin H, Howell HB, et al. Pharmacologic treatment of postpartum women with new-onset major depressive disorder: a randomized controlled trial with paroxetine. Journal of Clinical Psychiatry. 2008 Apr;69(4):659-65. PMID: 18363420.

Appendix C. Excluded Studies

The following full text articles were reviewed for inclusion but failed to meet inclusion criteria for reasons specified below.

1: Foreign language, 2: ineligible outcome, 3: ineligible intervention, 4: ineligible population, 5: ineligible publication type, 6: ineligible study design, 8: outdated or ineligible systematic review.

Study	Exclusion Code
1. St John's wort and depression: slight efficacy at best, many drug interactions. Prescrire International. 2004 Oct;13(73):187-92. PMID: 15499702	5
2. Neonatal complications after intrauterine exposure to SSRI antidepressants. Prescrire International. 2004 Jun;13(71):103-4. PMID: 15233148	5
3. Bupropion (amfebutamone): caution during pregnancy. Prescrire International. 2005 Dec;14(80):225. PMID: 16400747	5
4. Prenatal exposure to mirtazapine and birth outcomes. Brown University Child & Adolescent Psychopharmacology Update. 2006;8(10):5-. PMID: 2009312560. Language: English. Entry Date: 20080125. Publication Type: journal article. Journal Subset: Biomedical	5
5. Teratogenicity of SSRI antidepressants: study 2. Nurses' Drug Alert. 2007;31(8):45-6. PMID: 2009641186. Language: English. Entry Date: 20071207. Revision Date: 20101022. Publication Type: journal article	5
6. Selective serotonin reuptake inhibitors and birth defects. ACOG Clinical Review. 2008;13(2):12-3. PMID: 2009951120. Language: English. Entry Date: 20080718. Publication Type: journal article	5
7. Safety of SSRIs in pregnancy. Obstetrics and Gynecology. 2009;113(5):1162-7.	5
8. Study: Both SSRI use and depression in pregnancy linked to risky birth outcomes. Brown University Psychopharmacology Update. 2012;23(6):1-6. PMID: 2011552058. Language: English. Entry Date: 20120608. Revision Date: 20120608. Publication Type: journal article. Journal Subset: Biomedical	5
9. Ananth J. Congenital malformations with psychopharmacologic agents. Comprehensive Psychiatry. 1975 Sep-Oct;16(5):437-45. PMID: 240643	5
10. Andrade C. Selective serotonin reuptake inhibitors and persistent pulmonary hypertension of the newborn. Journal of Clinical Psychiatry. 2012 May;73(5):e601-5. PMID: 22697207	5
11. Andrade SE, Raebel MA, Brown J, et al. Use of antidepressant medications during pregnancy: a multisite study. American Journal of Obstetrics & Gynecology. 2008 Feb;198(2):194.e1-5. PMID: 17905176	2
12. Appleby L, Koren G, Sharp D. Depression in pregnant and postnatal women: an evidence-based approach to treatment in primary care. British Journal of General Practice. 1999 Oct;49(447):780-2. PMID: 10885079	5
13. Babu GN, Thippeswamy H, Chandra PS. Use of electroconvulsive therapy (ECT) in postpartum psychosis-a naturalistic prospective study. Arch Womens Ment Health. 2013 Apr 9;9:9.	3
14. Bar-Oz B, Einarson T, Einarson A, et al. Paroxetine and congenital malformations: meta-Analysis and consideration of potential confounding factors. Clinical Therapeutics. 2007 May;29(5):918-26. PMID: 17697910	8

Study	Exclusion Code
15. Bellantuono C, Migliarese G, Gentile S. Serotonin reuptake inhibitors in pregnancy and the risk of major malformations: a systematic review. Human Psychopharmacology. 2007 Apr;22(3):121-8. PMID: 17397101	6
16. Berard A. Paroxetine exposure during pregnancy and the risk of cardiac malformations: what is the evidence? Birth Defects Research. 2010 Mar;88(3):171-4. PMID: 19950383	5
17. Birnbaum CS, Cohen LS, Bailey JW, et al. Serum concentrations of antidepressants and benzodiazepines in nursing infants: A case series. Pediatrics. 1999 Jul;104(1):e11. PMID: 10390297	5
18. Blier P. Pregnancy, depression, antidepressants and breast-feeding. Journal of Psychiatry & Neuroscience. 2006 Jul;31(4):226-8. PMID: 16862240	5
19. Bodnar LM, Sunder KR, Wisner KL. Treatment with selective serotonin reuptake inhibitors during pregnancy: deceleration of weight gain because of depression or drug?.[Erratum appears in Am J Psychiatry. 2006 Oct;163(10):1843]. American Journal of Psychiatry. 2006 Jun;163(6):986-91. PMID: 16741197	5
20. Boucher N, Koren G, Beaulac-Baillargeon L. Maternal use of venlafaxine near term: correlation between neonatal effects and plasma concentrations. Therapeutic Drug Monitoring. 2009 Jun;31(3):404-9. PMID: 19455083	6
21. Bowen A, Bowen R, Butt P, et al. Patterns of depression and treatment in pregnant and postpartum women. Canadian Journal of Psychiatry. 2012;57(3):161-7.	6
22. Brandon AR. Ethical Barriers to Perinatal Mental Health Research and Evidence-Based Treatment: An Empirical Study. AJOB Primary Research. 2011 2011/01/01;2(1):2-12.	6
23. Bromley RL, Wieck A, Makarova D, et al. Fetal effects of selective serotonin reuptake inhibitor treatment during pregnancy: Immediate and longer term child outcomes. Fetal and Maternal Medicine Review. 2012;23(3-4):230-75.	8
24. Brosh K, Matok I, Sheine E, et al. Teratogenic determinants of first- trimester exposure to antiepileptic medications. Journal of Population Therapeutics and Clinical Pharmacology. 2011;18(1):e89-e98.	3
25. Burns A, O'Mahen H, Baxter H, et al. A pilot randomised controlled trial of cognitive behavioural therapy for antenatal depression. BMC Psychiatry. 2013 Jan 22;13(1):33.	3
26. Casper RC, Gilles AA, Fleisher BE, et al. Length of prenatal exposure to selective serotonin reuptake inhibitor (SSRI) antidepressants: effects on neonatal adaptation and psychomotor development. Psychopharmacology. 2011 Sep;217(2):211-9. PMID: 21499702	6
27. Chaudron LH. Complex challenges in treating depression during pregnancy. Am J Psychiatry. 2013 Jan 1;170(1):12-20. doi: 10.1176/appi.ajp.2012.12040440.	5
28. Cipriani A, Koesters M, Furukawa TA, et al. Duloxetine versus other anti-depressive agents for depression. Cochrane Database of Systematic Reviews. 2012(10)PMID: 00075320-100000000-05164	8
29. Cipriani A, Purgato M, Furukawa TA, et al. Citalopram versus other anti-depressive agents for depression. Cochrane Database of Systematic Reviews. 2012(7)PMID: 00075320-100000000-05154	8
30. Clementi M, Di Gianantonio E, Ornoy A. Teratology Information Services in Europe and Their Contribution to the Prevention of Congenital Anomalies. Public Health Genomics. 2002;5(1):8-12.	5
31. Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment.[Erratum appears in JAMA. 2006 Jul 12;296(2):170]. JAMA. 2006 Feb 1;295(5):499-507. PMID: 16449615	4

Study	Exclusion Code
32. Cohen LS, Altshuler LL, Stowe ZN, et al. Reintroduction of antidepressant therapy across pregnancy in women who previously discontinued treatment. A preliminary retrospective study. Psychotherapy & Psychosomatics. 2004 Jul-Aug;73(4):255-8. PMID: 15184721	4
33. Cohen LS, Heller VL, Bailey JW, et al. Birth outcomes following prenatal exposure to fluoxetine. Biological Psychiatry. 2000 Nov 15;48(10):996-1000. PMID: 11082474	6
34. Cohen LS, Nonacs RM, Bailey JW, et al. Relapse of depression during pregnancy following antidepressant discontinuation: a preliminary prospective study. Archives of Women's Mental Health. 2004 Oct;7(4):217-21. PMID: 15338315	4
35. Cohen LS, Rosenbaum JF. Birth outcomes in pregnant women taking fluoxetine. New England Journal of Medicine. 1997 Mar 20;336(12):872; author reply 3. PMID: 9072682	5
36. Cohen LS, Viguera AC, Bouffard SM, et al. Venlafaxine in the treatment of postpartum depression. Journal of Clinical Psychiatry. 2001 Aug;62(8):592-6. PMID: 11561929	6
37. Condon J. Serotonergic symptoms in neonates exposed to SSRIs during pregnancy. Australian & New Zealand Journal of Psychiatry. 2003 Dec;37(6):777-8. PMID: 14636401	5
38. Conlon O, Price J. A comparative study of pregnant women attending a tertiary obstetric unit and a district general hospital with a previous history of postnatal depression. Journal of Obstetrics & Gynaecology. 2006 Aug;26(6):514-7. PMID: 17000495	2
39. Courtney K. Use of SSRIs in pregnancy: neonatal implications. Nursing for Women's Health. 2009 Jun;13(3):234-8. PMID: 19523137	5
40. Coverdale JH, McCullough LB, Chervenak FA. The ethics of randomized placebo-controlled trials of antidepressants with pregnant women: a systematic review. Obstetrics & Gynecology. 2008 Dec;112(6):1361-8. PMID: 19037048	6
41. D C. OPEN-LABEL TRIAL OF ESCITALOPRAM IN WOMEN WITH POSTPARTUM MOOD AND ANXIETY DISORDERS. Primary Psychiatry. 2010;17(7):22-. PMID: 2011389039. Language: English. Entry Date: 20120106. Revision Date: 20120713. Publication Type: journal article	5
42. Davis RL, Andrade S, Platt R. Risk of congenital malformations among infants exposed to antidepressants during pregnancy. Pharmacoepidemiology and Drug Safety. 2008;17(4):423.	5
43. Dennis C-LE, Stewart DE. Treatment of postpartum depression, part 1: a critical review of biological interventions. Journal of Clinical Psychiatry. 2004 Sep;65(9):1242-51. PMID: 15367053	8
44. Desai G, Babu GN, Chandra PS. Unplanned pregnancies leading to psychotropic exposure in women with mental illness - Findings from a perinatal psychiatry clinic. Indian Journal of Psychiatry. 2012;54(1):59-63.	6
45. di Scalea TL, Wisner KL. Pharmacotherapy of postpartum depression. Expert Opinion on Pharmacotherapy. 2009 Nov;10(16):2593-607. PMID: 19874247	6
46. Dolk H, Jentink J, Loane M, et al. Does lamotrigine use in pregnancy increase orofacial cleft risk relative to other malformations? Neurology. 2008;71(10):714-22.	3
47. Einarson A, Fatoye B, Sarkar M, et al. Pregnancy outcome following gestational exposure to venlafaxine: a multicenter prospective controlled study. American Journal of Psychiatry. 2001 Oct;158(10):1728-30. PMID: 11579012	6
48. Einarson A, Koren G. Motherisk update: New antidepressants in pregnancy. Canadian Family Physician. 2004;50(FEB.):227-9.	5

Study	Exclusion Code
49. Einarson A, Pistelli A, DeSantis M, et al. Evaluation of the risk of congenital cardiovascular defects associated with use of paroxetine during pregnancy.[Erratum appears in Am J Psychiatry. 2008 Sep;165(9):1208], [Erratum appears in Am J Psychiatry. 2008 Jun;165(6):777]. American Journal of Psychiatry. 2008 Jun;165(6):749-52. PMID: 18381907	6
50. Einarson TR, Einarson A. Newer antidepressants in pregnancy and rates of major malformations: a meta-analysis of prospective comparative studies. Pharmacoepidemiology & Drug Safety. 2005 Dec;14(12):823-7. PMID: 15742359	8
51. Flynn HA, Blow FC, Marcus SM. Rates and predictors of depression treatment among pregnant women in hospital-affiliated obstetrics practices. General Hospital Psychiatry. 2006;28(4):289-95.	2
52. Freeman MP. New data inform the risk/benefit analysis in antenatal depression. Journal of Clinical Psychiatry. 2007 Aug;68(8):1277-8. PMID: 17854253	5
53. Freeman MP. Complementary and alternative medicine for perinatal depression. Journal of Affective Disorders. 2009;112(1-3):1-10.	5
54. Galanti M, Jeffrey Newport D, Pennell PB, et al. Postpartum depression in women with epilepsy: Influence of antiepileptic drugs in a prospective study. Epilepsy and Behavior. 2009;16(3):426-30.	3
55. Galbally M, Gentile S, Lewis AJ. Further findings linking SSRIs during pregnancy and persistent pulmonary hypertension of the newborn: Clinical implications. CNS Drugs. 2012;26(10):813-22.	5
56. Gentile S. SSRIs in pregnancy and lactation: emphasis on neurodevelopmental outcome. CNS Drugs. 2005;19(7):623-33. PMID: 15984897	5
57. Gentile S. The safety of newer antidepressants in pregnancy and breastfeeding. Drug Safety. 2005;28(2):137-52. PMID: 15691224	5
58. Gentile S. Serotonin reuptake inhibitor-induced perinatal complications. Paediatric Drugs. 2007;9(2):97-106. PMID: 17407365	5
59. Gentile S. On categorizing gestational, birth, and neonatal complications following late pregnancy exposure to antidepressants: the prenatal antidepressant exposure syndrome. Cns Spectrums. 2010 Mar;15(3):167-85. PMID: 20414166	6
60. Gentile S. Neonatal Withdrawal Reactions Following Late in Utero Exposure to Antidepressant Medications. Current Women's Health Reviews. 2011;7(1):18-27. PMID: 2011195182. Language: English. Entry Date: 20110729. Revision Date: 20120706. Publication Type: journal article	6
61. Gentile S. Selective serotonin reuptake inhibitor exposure during early pregnancy and the risk of birth defects. Acta Psychiatrica Scandinavica. 2011 Apr;123(4):266-75. PMID: 21261600	5
62. Gentile S, Bellantuono C. Selective serotonin reuptake inhibitor exposure during early pregnancy and the risk of fetal major malformations: focus on paroxetine. Journal of Clinical Psychiatry. 2009 Mar;70(3):414-22. PMID: 19254517	5
63. Gentile S, Galbally M. Prenatal exposure to antidepressant medications and neurodevelopmental outcomes: a systematic review. Journal of Affective Disorders. 2011 Jan;128(1-2):1-9. PMID: 20303599	5
64. Gjerdingen D. The effectiveness of various postpartum depression treatments and the impact of antidepressant drugs on nursing infants. Journal of the American Board of Family Practice. 2003 Sep-Oct;16(5):372-82. PMID: 14645327	5
65. Gold KJ, Marcus SM. Effect of maternal mental illness on pregnancy outcomes. Expert Review of Obstetrics and Gynecology. 2008;3(3):391-401.	5

Study	Exclusion Code
66. Goldfarb C, Keating G. Use of antidepressants from conception to delivery. Journal of the Medical Society of New Jersey. 1981 May;78(5):357-60. PMID: 6945438	5
67. Goldstein DJ, Corbin LA, Sundell KL. Effects of first-trimester fluoxetine exposure on the newborn. Obstetrics & Gynecology. 1997 May;89(5 Pt 1):713-8. PMID: 9166307	6
68. Grush LR, Cohen LS. Treatment of depression during pregnancy: balancing the risks. Harvard Review of Psychiatry. 1998 Jul-Aug;6(2):105-9. PMID: 10370454	5
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70. Haller E. Depression during and after pregnancy: what does the primary care physician need to know? Johns Hopkins Advanced Studies in Medicine. 2005;5(1):21-6. PMID: 2005107077. Language: English. Entry Date: 20050715. Revision Date: 20090313. Publication Type: journal article	5
71. Hemels MEH, Einarson A, Koren G, et al. Antidepressant use during pregnancy and the rates of spontaneous abortions: a meta-analysis. Annals of Pharmacotherapy. 2005 May;39(5):803-9. PMID: 15784808	8
72. Hendrick V, Altshuler L. Management of major depression during pregnancy. American Journal of Psychiatry. 2002 Oct;159(10):1667-73. PMID: 12359670	5
73. Hendrick V, Altshuler L, Strouse T, et al. Postpartum and nonpostpartum depression: differences in presentation and response to pharmacologic treatment. Depression & Anxiety. 2000;11(2):66-72. PMID: 10812531	4
74. Hendrick V, Smith LM, Hwang S, et al. Weight gain in breastfed infants of mothers taking antidepressant medications. Journal of Clinical Psychiatry. 2003 Apr;64(4):410-2. PMID: 12716242	6
75. Hendrick V, Smith LM, Suri R, et al. Birth outcomes after prenatal exposure to antidepressant medication. American Journal of Obstetrics & Gynecology. 2003 Mar;188(3):812-5. PMID: 12634662	6
76. Highet N, Drummond P. A comparative evaluation of community treatments for post-partum depression: Implications for treatment and management practices. Australian and New Zealand Journal of Psychiatry. 2004;38(4):212-8.	2
77. Hilli J, Heikkinen T, Rontu R, et al. MAO-A and COMT genotypes as possible regulators of perinatal serotonergic symptoms after in utero exposure to SSRIs. European Neuropsychopharmacology. 2009 May;19(5):363-70. PMID: 19223155	6
78. Hoffbrand S, Howard L, Crawley H. Antidepressant treatment for post-natal depression. Nursing Times. 2001 Nov 8-14;97(45):35. PMID: 11966146	5
79. Hoffbrand S, Howard L, Crawley H. Antidepressant drug treatment for postnatal depression. Cochrane Database of Systematic Reviews. 2001(2):CD002018. PMID: 11406023	8
80. Howard L. Postnatal depression. Clinical Evidence. 2004 Dec(12):2000-15. PMID: 15865767	4
81. Howard L. Postnatal depression. Clinical Evidence. 2005 Dec(14):1764-75. PMID: 16620472	8
82. Howard L. Postnatal depression. Clinical Evidence. 2006 Jun(15):1919-31. PMID: 16973070	6
83. Howard LM, Hoffbrand S, Henshaw C, et al. Antidepressant prevention of postnatal depression. Cochrane Database of Systematic Reviews. 2005(2):CD004363. PMID: 15846711	8
84. Huang H, Chan Y, Katon W, et al. Variations in depression care and outcomes among high-risk mothers from different racial/ethnic groups. Family Practice. 2012;29(4):394-400.	6

Study	Exclusion Code
85. Hunter SK, Mendoza JH, D'Anna K, et al. Antidepressants may mitigate the effects of prenatal maternal anxiety on infant auditory sensory gating. American Journal of Psychiatry. 2012 Jun;169(6):616-24. PMID: 22581104	2
86. Jermain DM. Treatment of postpartum depression. American Pharmacy. 1995 Jan;NS35(1):33-8. PMID: 7887372	5
87. Kellner CH, Pasculli RM, Briggs MC. Treatment of depression during pregnancy. Journal of ECT. 2012;28(3):195-6.	5
88. Kendall-Tackett K, Hale TW. The use of antidepressants in pregnant and breastfeeding women: a review of recent studies. Journal of Human Lactation. 2010 May;26(2):187-95. PMID: 19652194	8
89. Koke SC, Brown EB, Miner CM. Safety and efficacy of fluoxetine in patients who receive oral contraceptive therapy. American Journal of Obstetrics and Gynecology. 2002;187(3):551-5.	4
90. Koren G. SSRIs in early pregnancy were associated with increased risk for septal heart defects but not major congenital malformations overall. ACP Journal Club. 2009;151(6):13-. PMID: 2010610620. Language: English. Entry Date: 20100430. Revision Date: 20100430. Publication Type: journal article	5
91. Koren G. The effect of ascertainment bias in evaluating gestational antidepressant exposure. Journal of Population Therapeutics and Clinical Pharmacology. 2011;18(1):e174-e5.	5
92. Koren G. SSRIs and persistent pulmonary hypertension in newborns. Brown University Psychopharmacology Update. 2012;23(5):7-8. PMID: 2011520008. Language: English. Entry Date: 20120504. Revision Date: 20120615. Publication Type: journal article. Journal Subset: Biomedical	5
93. Koren G, Boucher N. Adverse effects in neonates exposed to SSRIs and SNRI in late gestation--Motherisk Update 2008. Canadian Journal of Clinical Pharmacology. 2009;16(1):e66-7. PMID: 19164848	5
94. Koren G, Nordeng H. Antidepressant use during pregnancy: The benefit-risk ratio. American Journal of Obstetrics and Gynecology. 2012;207(3):157-63.	5
95. Koren G, Nordeng H. SSRIs and persistent pulmonary hypertension of the newborn: Observational evidence suggests a link, but causation is yet to be established. BMJ (Online). 2012;344(7842)	6
96. Koren G, Nulman I, Addis A. Outcome of children exposed in utero to fluoxetine: a critical review. Depression & Anxiety. 1998;8 Suppl 1:27-31. PMID: 9809211	5
97. Krebs C. Depression in pregnancy. Evidence-Based Practice. 2010;13(10):9. PMID: 2010920999. Language: English. Entry Date: 20110218. Publication Type: journal article	5
98. Kwon P, Lefkowitz W. Neonatal extrapyramidal movements. Neonatal withdrawal due to maternal citalopram and ondansetron use. Pediatric Annals. 2008 Mar;37(3):128-30. PMID: 18411854	5
99. Lanza di Scalea T, Wisner KL. Antidepressant medication use during breastfeeding. Clinical Obstetrics & Gynecology. 2009 Sep;52(3):483-97. PMID: 19661763	6
100. Lewis JD, Schinnar R, Bilker WB, et al. Validation studies of the health improvement network (THIN) database for pharmacoepidemiology research. Pharmacoepidemiology and Drug Safety. 2007;16(4):393-401.	5
101. Logsdon MC, Wisner K, Hanusa BH, et al. Role functioning and symptom remission in women with postpartum depression after antidepressant treatment. Archives of Psychiatric Nursing. 2003 Dec;17(6):276-83. PMID: 14685952	3

Study	Exclusion Code
102. Lopez-Yarto M, Ruiz-Mirazo E, Holloway AC, et al. Do psychiatric medications, especially antidepressants, adversely impact maternal metabolic outcomes? Journal of Affective Disorders. 2012 Dec;141(2-3):120-9. PMID: Peer Reviewed Journal: 2012-05505-001	8
103. Lorenzo L, Byers B, Einarson A. Antidepressant use in pregnancy. Expert Opinion on Drug Safety. 2011 Nov;10(6):883-9. PMID: 21545242	5
104. Loughhead AM, Stowe ZN, Newport DJ, et al. Placental passage of tricyclic antidepressants. Biological Psychiatry. 2006 Feb 1;59(3):287-90. PMID: 16271264	6
105. MacQueen GM, Ramakrishnan K, Ratnasingan R, et al. Desipramine treatment reduces the long-term behavioural and neurochemical sequelae of early-life maternal separation. International Journal of Neuropsychopharmacology. 2003;6(4):391-6.	6
106. Malm H. Prenatal exposure to selective serotonin reuptake inhibitors and infant outcome. Therapeutic Drug Monitoring. 2012;34(6):607-14.	5
107. Malm H, Klaukka T, Neuvonen PJ. Risks associated with selective serotonin reuptake inhibitors in pregnancy. Obstetrics & Gynecology. 2005 Dec;106(6):1289-96. PMID: 16319254	4
108. Marcus SM, Flynn HA. Depression, antidepressant medication, and functioning outcomes among pregnant women. International Journal of Gynaecology & Obstetrics. 2008 Mar;100(3):248-51. PMID: 18005968	6
109. Misri S, Kendrick K. Treatment of perinatal mood and anxiety disorders: a review. Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie. 2007 Aug;52(8):489-98. PMID: 17955910	6
110. Morrison JL, Riggs KW, Rurak DW. Fluoxetine during pregnancy: Impact on fetal development. Reproduction, Fertility and Development. 2005;17(6):641-50.	5
111. Morrow AW. Imipramine and congenital abnormalities. New Zealand Medical Journal. 1972 Apr;75(479):228-9. PMID: 4503545	5
112. Moses-Kolko EL, Bogen D, Perel J, et al. Neonatal signs after late in utero exposure to serotonin reuptake inhibitors: literature review and implications for clinical applications. JAMA. 2005 May 18;293(19):2372-83. PMID: 15900008	6
113. Murthy L, Shepperd S, Clarke MJ, et al. Interventions to improve the use of systematic reviews in decision-making by health system managers, policy makers and clinicians. Cochrane Database of Systematic Reviews. 2012(9)PMID: 00075320-100000000-07759	3
114. Ng RC, Hirata CK, Yeung W, et al. Pharmacologic treatment for postpartum depression: a systematic review. Pharmacotherapy:The Journal of Human Pharmacology & Drug Therapy. 2010 Sep;30(9):928-41. PMID: 20795848	6
115. No authorship i. Maternal SSRI Use Associated with Neurobehavioral Disruptions in Neonates. Primary Psychiatry. 2004 Apr;11(4):14-5. PMID: Peer Reviewed Journal: 2004-95123-004	4
116. No authorship i. Depression, SSRIs, and premature birth. The American Journal of Psychiatry. 2009 May;166(5):A22. PMID: Peer Reviewed Journal: 2009-09562-001	5
117. Oberlander TF, Grunau RE, Fitzgerald C, et al. Pain reactivity in 2-month-old infants after prenatal and postnatal serotonin reuptake inhibitor medication exposure. Pediatrics. 2005 Feb;115(2):411-25. PMID: 15687451	2
118. O'Brien LA-M. Critical determinants of the risk-benefit assessment of antidepressants in pregnancy: Pharmacokinetic, safety and economic considerations. Dissertation Abstracts International: Section B: The Sciences and Engineering. 2010;70(10-B):6133. PMID: Dissertation Abstract: 2010-99080-145	2

Study	Exclusion Code
119. O'Mahen H, Himle JA, Fedock G, et al. A Pilot Randomized Controlled Trial of Cognitive Behavioral Therapy for Perinatal Depression Adapted for Women with Low Incomes. Depression & Anxiety. 2013 Jan 14;14(10):22050.	3
120. Oyebode F, Rastogi A, Berrisford G, et al. Psychotropics in pregnancy: safety and other considerations. Pharmacology & Therapeutics. 2012 Jul;135(1):71-7. PMID: 22483705	6
121. Pupco A, Bozzo P, Koren G. Selective serotonin reuptake inhibitors and risk for major congenital anomalies. Obstetrics and Gynecology. 2011;118(4):959-60.	5
122. Rahimi R, Nikfar S, Abdollahi M. Pregnancy outcomes following exposure to serotonin reuptake inhibitors: a meta-analysis of clinical trials. Reproductive Toxicology. 2006;22(4):571-5.	6
123. Raudzus J, Misri S. Managing unipolar depression in pregnancy. Current Opinion in Psychiatry. 2009 Jan;22(1):13-8. PMID: 19122529	6
124. Reefhuis J, Rasmussen SA, Friedman JM. Selective serotonin-reuptake inhibitors and persistent pulmonary hypertension of the newborn. New England Journal of Medicine. 2006 May 18;354(20):2188-90; author reply -90. PMID: 16707761	5
125. Richards EM, Payne JL. The management of mood disorders in pregnancy: alternatives to antidepressants. CNS Spectrums. 2013;FirstView:1-11.	5
126. Ricke AK, Farrell CE, Chambers JE. The pharmacotherapy of perinatal mood disorders. Psychopharm Review. 2009;44(10):73-80.	5
127. Roca A, Garcia-Esteve L, Imaz ML, et al. Obstetrical and neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitors: the relevance of dose. Journal of Affective Disorders. 2011 Dec;135(1-3):208-15. PMID: 21890210	6
128. Ross EL, Grigoriadis S, Mamisashvili L. Selected pregnancy and delivery outcomes after exposure to antidepressant medication: A systematic review and meta-analysis. JAMA Psychiatry. 2013:1-8.	8
129. Ruchkin V, Martin A. SSRIs and the developing brain. Lancet. 2005 Feb 5-11;365(9458):451-3. PMID: 15705440	5
130. Santone G, Ricchi G, Rocchetti D, et al. Is the exposure to antidepressant drugs in early pregnancy a risk factor for spontaneous abortion? A review of available evidences. Epidemiologia e Psichiatria Sociale. 2009;18(3):240-7.	6
131. Santos F, Sola I, Rigau D, et al. Quality assessment of clinical practice guidelines for the prescription of antidepressant drugs during pregnancy. Current Clinical Pharmacology. 2012 Feb 1;7(1):7-14. PMID: 22299765	5
132. Sanz EJ, De-las-Cuevas C, Kiuru A, et al. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: a database analysis. Lancet. 2005 Feb 5-11;365(9458):482-7. PMID: 15705457	6
133. Schroeder JW, Smith AK, Brennan PA, et al. DNA methylation in neonates born to women receiving psychiatric care. Epigenetics: Official Journal of the DNA Methylation Society. 2012 Apr;7(4):409-14. PMID: 22419064	2
134. Seifritz E, Holsboer-Trachsler E, Haberthur F, et al. Unrecognized pregnancy during citalopram treatment. American Journal of Psychiatry. 1993 Sep;150(9):1428-9. PMID: 8352360	5
135. Shea AK, Kamath MV, Fleming A, et al. The effect of depression on heart rate variability during pregnancy. A naturalistic study. Clinical Autonomic Research. 2008 Aug;18(4):203-12. PMID: 18592128	3

Study	Exclusion Code
136. Silvani P, Camporesi A. Drug-induced pulmonary hypertension in newborns: A review. Current Vascular Pharmacology. 2007;5(2):129-33.	5
137. Simoncelli M, Martin B-Z, Berard A. Antidepressant use during pregnancy: a critical systematic review of the literature. Current Drug Safety. 2010 Apr;5(2):153-70. PMID: 19534639	6
138. Sockol LE, Epperson CN, Barber JP. A meta-analysis of treatments for perinatal depression. Clinical Psychology Review. 2011 Jul;31(5):839-49. PMID: 21545782	6
139. Sontheimer DL, Ables AZ. Safety of antidepressant medications during pregnancy. JAMA. 2000 Mar 1;283(9):1139. PMID: 10703770	5
140. Speisman BB, Storch EA, Abramowitz JS. Postpartum obsessive-compulsive disorder. JOGNN - Journal of Obstetric, Gynecologic, & Neonatal Nursing. 2011 Nov-Dec;40(6):680-90. PMID: 22092284	4
141. Steinberg SI, Bellavance F. Characteristics and treatment of women with antenatal and postpartum depression. International Journal of Psychiatry in Medicine. 1999;29(2):209-33. PMID: 10587816	2
142. Stewart DE. Are there special considerations in the prescription of serotonin reuptake inhibitors for women? Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie. 1998 Nov;43(9):900-4. PMID: 9825160	5
143. Stowe ZN. The use of mood stabilizers during breastfeeding. Journal of Clinical Psychiatry. 2007;68(SUPPL. 9):22-8.	5
144. Strom M, Mortensen EL, Halldorson TI, et al. Leisure-time physical activity in pregnancy and risk of postpartum depression: a prospective study in a large national birth cohort. Journal of Clinical Psychiatry. 2009 Dec;70(12):1707-14. PMID: 20141710	2
145. Sunder KR, Wisner KL, Hanusa BH, et al. Postpartum depression recurrence versus discontinuation syndrome: observations from a randomized controlled trial. Journal of Clinical Psychiatry. 2004 Sep;65(9):1266-8. PMID: 15367055	4
146. t Jong GW, Einarson T, Koren G, et al. Antidepressant use in pregnancy and persistent pulmonary hypertension of the newborn (PPHN): A systematic review. Reproductive Toxicology. 2012;34(3):293-7.	8
147. Ter Horst P, Smit J. Antidepressants during pregnancy and lactation. Tijdschrift voor Psychiatrie. 2009;51(5):307-14. PMID: Peer Reviewed Journal: 2011-28846-003	1
148. Thompson BL, Levitt P, Stanwood GD. Prenatal exposure to drugs: effects on brain development and implications for policy and education. Nature Reviews Neuroscience. 2009 Apr;10(4):303-12. PMID: 19277053	5
149. Thormahlen GM. Paroxetine use during pregnancy: is it safe? Annals of Pharmacotherapy. 2006 Oct;40(10):1834-7. PMID: 16926304	5
150. Tuccori M, Montagnani S, Testi A, et al. Use of selective serotonin reuptake inhibitors during pregnancy and risk of major and cardiovascular malformations: an update. Postgraduate Medicine. 2010 Jul;122(4):49-65. PMID: 20675971	5
151. Tuccori M, Testi A, Antonioli L, et al. Safety concerns associated with the use of serotonin reuptake inhibitors and other serotonergic/noradrenergic antidepressants during pregnancy: a review. Clinical Therapeutics. 2009 Jun;31 Pt 1:1426-53. PMID: 19698902	5
152. Udechuku A, Nguyen T, Hill R, et al. Antidepressants in pregnancy: a systematic review. Australian & New Zealand Journal of Psychiatry. 2010 Nov;44(11):978-96. PMID: 21034181	5

Study	Exclusion Code
153. Ververs T, Kaasenbrood H, Visser G, et al. Prevalence and patterns of antidepressant drug use during pregnancy. European Journal of Clinical Pharmacology. 2006 Oct;62(10):863-70. PMID: 16896784	2
154. Warburton W, Hertzman C, Oberlander TF. A register study of the impact of stopping third trimester selective serotonin reuptake inhibitor exposure on neonatal health. Acta Psychiatrica Scandinavica. 2010 Jun;121(6):471-9. PMID: 19878137	6
155. Watanabe N, Omori IM, Nakagawa A, et al. Mirtazapine versus other antidepressive agents for depression. Cochrane Database of Systematic Reviews. 2011(12)PMID: 00075320-100000000-05204	8
156. Weikum WM, Oberlander TF, Hensch TK, et al. Prenatal exposure to antidepressants and depressed maternal mood alter trajectory of infant speech perception. PNAS Proceedings of the National Academy of Sciences of the United States of America. 2012 Oct;109(Suppl 2):17221-7. PMID: Peer Reviewed Journal: 2012-28317-012	5
157. Wenstrom KD. [Commentary on] Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. Obstetrical & Gynecological Survey. 2006;61(6):370-1. PMID: 2009217667. Language: English. Entry Date: 20060929. Revision Date: 20070105. Publication Type: journal article	5
158. Werler MM, Bower C, Payne J, et al. Findings on potential teratogens from a case-control study in Western Australia. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2003;43(6):443-7.	3
159. Wisner KL, Gelenberg AJ, Leonard H, et al. Pharmacologic treatment of depression during pregnancy. JAMA. 1999 Oct 6;282(13):1264-9. PMID: 10517430	6
160. Wisner KL, Perel JM, Peindl KS, et al. Prevention of postpartum depression: a pilot randomized clinical trial. American Journal of Psychiatry. 2004 Jul;161(7):1290-2. PMID: 15229064	4
161. Wu J, Viguera A, Riley L, et al. Mood disturbance in pregnancy and the mode of delivery. American Journal of Obstetrics and Gynecology. 2002;187(4):864-7.	6
162. Wurst KE, Poole C, Ephross SA, et al. First trimester paroxetine use and the prevalence of congenital, specifically cardiac, defects: a meta-analysis of epidemiological studies. Birth Defects Research. 2010 Mar;88(3):159-70. PMID: 19739149	8
163. Yaris F, Ulku C, Kesim M, et al. Psychotropic drugs in pregnancy: A case-control study. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2005;29(2):333-8.	1
164. Yonkers KA, Gotman N, Smith MV, et al. Does antidepressant use attenuate the risk of a major depressive episode in pregnancy? Epidemiology. 2011 Nov;22(6):848-54. PMID: 21900825	4
165. Zeskind PS. [Commentary on] Maternal selective serotonin reuptake inhibitor use during pregnancy and newborn neurobehavior. Obstetrical & Gynecological Survey. 2004;59(8):564-6. PMID: 2004161864. Language: English. Entry Date: 20041001. Publication Type: journal article	5
166. Zhou S, Chan E, Pan SQ, et al. Pharmacokinetic interactions of drugs with St John's wort. Journal of Psychopharmacology. 2004;18(2):262-76.	5
167. Zuccotti GV, Fabiano V, Manfredini V. Neonates born to mothers using antidepressant drugs. Early Human Development. 2012;88(SUPPL.2):S84-S5.	5

Appendix D. Studies Pending Review

1. Grigoriadis S, VonderPorten EH, Mamisashvili L. Antidepressant Exposure During Pregnancy and Congenital Malformations: Is There an Association? A Systematic Review and Meta-Analysis of the Best Evidence. J Clin Psychiatry. 2013 April;74(4):e293-e308. PMID: 23656855.

2. Grigoriadis S, VonderPorten EH, Mamisashvili L. The Effect of Prenatal Antidepressant Exposure on Neonatal Adaptation: A Systematic Review and Meta-Analysis. J Clin Psychiatry. 2013 April;74(4):e309-e20. PMID: 23656856.

3. Grigoriadis S, VonderPorten EH, Mamisashvili L. The Impact of Maternal Depression During Pregnancy on Perinatal Outcomes: A Systematic Review and Meta-Analysis. J Clin Psychiatry. 2013 April;74(4):e321-e41. PMID: 23656857.

4. Painuly N, Heun R, Painuly R, et al. Risk of cardiovascular malformations after exposure to paroxetine in pregnancy: meta analysis. The Psychiatrist. 2013;37(6):198-203.

5. Russell EJ, Fawcett JM, Mazmanian D. Risk of Obsessive-Compulsive Disorder in Pregnant and Postpartum Women: A Meta-Analysis. Journal of Clinical Psychiatry. 2013;74(4):377-85. PMID: 23656845.

6. Wisner KL, Bogen DL, Sit D, et al. Does Fetal Exposure to SSRIs or Maternal Depression Impact Infant Growth? Am J Psychiatry. 2013 May 1;170(5):485-93.

Appendix E. Strength of Evidence

Key Question 1a. Maternal and Child Benefits: Pharmacotherapy compared with placebo or no treatment

Table 1. Fluoxetine compared with no treatment during pregnancy

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Depression Symptomotology: Mean CES-D Score[1]						
1; N=46	High (1Observational/High)	Unknown	Direct	Unknown	Third trimester: 14.33 vs 25.93; *P*=0.0010	Insufficient

Table 2. SSRIs compared with no treatment during pregnancy

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Functional capacity: SF-12 mental component score[2]						
1; N=62	Medium (1Observational/Medium)	Unknown	Direct	Unknown	45.2 vs 35.3, post-hoc Scheffé tests described as showing a significant difference, but results not reported	Insufficient
Preterm birth[3]						
1; N=200	Medium (1Observational/Medium)	Unknown	Direct	Imprecise	Unadjusted OR 1.73 (95% CI; 0.63-4.42)	Insufficient
Infant/Child Development: Brazelton Neonatal Behavioral Assessment Scale[4]						
1; N=49	Medium (1Observational/Medium)	Unknown	Direct	Unknown	No significant differences on any summary scores for 7 major clusters	Insufficient

Table 3. Paroxetine compared with placebo during the postpartum period[5]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological Limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Danger to self						
1; 70	High (RCT/High)	Unknown	Direct	Imprecise	No episodes	Insufficient
Danger to infant						

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
1; 70	High (RCT/High)	Unknown	Direct	Imprecise	No episodes	Insufficient
Depression response[1]						
1; 70	High (RCT/High)	Unknown	Direct	Imprecise	OR 1.31 (0.50-3.41)	Insufficient
Depression remission[2]						
1; 70	High (RCT/High)	Unknown	Direct	Precise	OR 3.54 (1.10-11.41)	Insufficient
Breastfeeding						
NA	NA	NA	NA	NA	No evidence	Insufficient
Weight gain						
NA	NA	NA	NA	NA	No evidence	Insufficient

[1] Response at week 8 as measured by Clinical Global Impression-Improvement (CGI-I) of 1 or 2.
[2] Remission by week 8 as measured by the 17 Item Hamilton rating Scale for Depression (HAM-D-17) ≤ 8.

Key Question 1b. Maternal and Child Benefits: Pharmacological treatments compared with each other

Table 4. Sertraline compared with nortriptyline during the postpartum period

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological Limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Depression response[1 6]						
1; 109	High (RCT/High)	Unknown	Direct	Imprecise	Week 4: OR 0.79 (0.28-2.19)	Insufficient
				Imprecise	Week 8: OR 0.99 (0.29-3.42)	Insufficient
Depression remission[2 6]						
1; 109	High (RCT/High)	Unknown	Direct	Imprecise	Week 4: OR 1.04 (0.41-2.65)	Insufficient
				Imprecise	Week 8: OR 1.75 (0.69-4.38)	Insufficient
Intention to Breastfeed						
	NA	NA	NA	NA	No evidence	Insufficient
Duration of Breastfeeding[3 7]						
1; 70	High (RCT/High)	Unknown	Direct	Imprecise	Week 8: OR 2.78 (0.86-8.94)	Insufficient
Weight gain						
NA	NA	NA	NA	NA	No evidence	Insufficient

[1] Response is considered >= 50% reduction in Hamilton Rating Scale for Depression (HSRD) .
[2] Remission is considered a Hamilton Rating Scale for Depression (HRDS) <7.
[3] Reported as breast feeding yes or no at 8th week of study.

Key Question 1d2. Maternal and Child Benefits: Pharmacological treatments plus nonpharmacological treatment compared with nonpharmacological treatments alone

Table 5. SSRIs plus psychotherapy compared with psychotherapy alone during pregnancy[8]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Depression Symptomotology: BDI maximum score[8]						
1; N=44	Medium (1Observational/Medium)	Unknown	Direct	Imprecise	21.3 vs 24.0; *P*=0.58	insufficient
Breastfeeding: Mean duration in months						
1; N=44	Medium (Observational/Medium)	Unknown	Direct	Imprecise	8.5 vs 6.4; *P* = 0.4	Insufficient

Table 6. Sertraline and brief dynamic psychotherapy compared with brief psychodynamic psychotherapy during the postpartum period[9]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological Limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Depression response[1]						
1; 40	Medium (RCT/Medium)	Unknown	Direct	Imprecise	Week 8: OR 1.91 (0.52-7.00)	Low
Depression remission[2]						
1; 40	Medium (RCT/Medium)	Unknown	Direct	Imprecise	Week 8: OR 3.09 (0.78-12.14)	Low
				Imprecise	Week 12: OR 3.64 (0.34-39.02)	Low

[1] Response was defined as >50% reduction in MADRS or EPDS scores.
[2] Remission was considered as final score on the MADRS of <10 or the EPDS <7.

Table 7. Paroxetine plus cognitive behavioral therapy compared with cognitive behavioral therapy alone during the postpartum period[10]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological Limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Depression response[1, 2]**:**						
1; 87	Medium (RCT/Medium)	NA	NA	NA	No evidence	Insufficient

Key Question 1d3. Maternal and Child Benefits: Comparing Pharmacological Treatments Alone with Pharmacological Treatments Used in Combination with Nonpharmacological Treatments

Table 8. Paroxetine compared with paroxetine plus cognitive behavioral therapy during the postpartum period[11]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological Limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Depression response[1, 2]:						
1; 35	Medium (RCT/Medium)	Unknown	Direct	Imprecise	HAM-D[1]: OR 1.87 (0.29-11.84)	Low
				Imprecise	EPDS[2]: OR 2.71 (0.73-10.04)	Low

[1]Response on Hamilton Rating Scale for Depression (HAM-D) (>= 50% score reduction).
[2]Response on Edinburgh Post Natal Depression Scale is (EDPS) (>= 50% score reduction).

Table 9. Sertraline compared with sertraline plus interpersonal psychotherapy during the postpartum period[12]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological Limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Depression response						
1; 23	High (RCT/High)	Unknown	Direct	Imprecise	No significant differences *	Insufficient
Depression remission						
1; 23	High (RCT/High)	Unknown	Direct	Imprecise	No significant differences *	Insufficient

* ANCOVA adjusted for pretreatment depression

Key Question 2a. Maternal and Child Harms: Pharmacotherapy compared with placebo or no treatment

Table 10. SSRIs compared with no treatment during pregnancy

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	**Methodological limitations**	**Consistency**	**Directness**	**Precision**	**Summary effect size (95% CI)**	**High, moderate, low, insufficient**
Major malformations[2]						
1; N=72	Medium (1 Observational/Medium)	Unknown	Direct	Imprecise	No events	Insufficient
Convulsions[13]						
1; N=15,685	Medium (1 observational/Medium)	Unknown	Direct	Precise	0.14% vs 0.11%; RD 0.0005; 95% CI, -0.0015 to 0.0025)	Low
Respiratory Distress[2, 8, 13]						
3;	Medium (3	Consistent	Direct	Precise	Pooled	Low

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
N=15,793	observational/Medium)				unadjusted OR 1.91 (95% CI, 1.63 to 2.24)	

Table 11. Bupropion compared with no treatment during pregnancy

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Major malformations[14]						
1; N=126	High (1 Observational/ High)	Unknown	Direct	Imprecise	No events	Insufficient

Key Question 2b. Maternal and Child Harms: Pharmacological treatments compared with each other

Table 12. SSRI's compared with TCAs (nortriptyline) during pregnancy

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Respiratory Distress[15]						
1; N=21	Medium (1Observational/Medium)	Unknown	Direct	Imprecise	10% vs 0%; *P* not reported	Insufficient

Table 13. SSRI's compared with SSRIs during pregnancy

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Respiratory Distress[15]						
1; N=20	Medium (1Observational/Medium)	Unknown	Direct	Imprecise	22% vs 0%, *P*=NR	Insufficient

Table 14. Sertraline compared with nortriptyline during the postpartum period[6]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Overall adverse events and withdrawals due to adverse events						
1; N=109	High (1Observational/High)	Unknown	Direct	Imprecise	No events	Insufficient

Key Question 2d2. Maternal and Child Harms: Pharmacological treatments plus nonpharmacological treatment compared with nonpharmacological treatments alone

Table 15. SSRIs plus psychotherapy compared with psychotherapy alone during pregnancy[8]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Major malformations						
1; N=44	Medium (Observational/Medium)	Unknown	Direct	Imprecise	Unadjusted OR 0.40; 95% CI, 0.02 to 6.93	Insufficient

Table 16 Sertraline and brief dynamic psychotherapy compared with brief psychodynamic psychotherapy during the postpartum period[9]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological Limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
% Discontinuing due to adverse events						
1; 40	Medium (RCT/Medium)	Unknown	Direct	Precise	OR 5.54 (0.25-123.09)	Insufficient

Table 17. Fluoxetine plus cognitive behavioral therapy compared with cognitive behavioral therapy alone during the postpartum period[10]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological Limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
% Discontinuing due to adverse events						
1; 87	Medium (RCT/Medium)	Unknown	Direct	Imprecise	1 session: 0% vs 9%; *P* not reported 6 sessions: 5% vs 5%; *P* not reported	Insufficient

Table 18. Sertraline plus interpersonal therapy compared with interpersonal therapy alone during the postpartum period[12]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological Limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
% Discontinuing due to adverse events						
1; 23	High (RCT/High)	Unknown	Direct	Imprecise	No events	Insufficient

Key Question 2d3. Maternal and Child Harms: Pharmacological treatments alone compared with pharmacologicala treatments plus nonpharmacological treatments

Table 19. Sertraline alone compared with sertraline plus interpersonal therapy during the postpartum period[12]

Domains pertaining to strength of evidence					Magnitude of effect	Strength of evidence
Number of studies; Number of subjects	Methodological Limitations	Consistency	Directness	Precision	Summary effect size (95% CI)	High, moderate, low, insufficient
Overall adverse events						
1; 23	High (RCT/High)	Unknown	Direct	Imprecise	No events	Insufficient

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Appendix F. Evidence Tables

Evidence Table 1. Data Abstraction of Observational Studies

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Alwan 2007[1] US Arm of Case Control Studied, Population based Medium	Race: W: 60.5%; AA: 11%, Hisp 23%, other 5.5%. Age: <35y: 84%/>35y: 15%. Income: 20K: 32%/20-4999: 32.5%/ >50K: 35% Home: NR; Planned Pg: NR; Partner NR	Mental health comorbidities: NR. Other meds: , 1%; Prov Chara: NR; Med Care env: NR	% Dx: NR; Fam Hx NR; Prior use: NR; Sx Severity NR; Time of Dx NR; Dx method: NR. Tx began: before pg/during pg.
Alwan 2010[2] Canada Case-control/Data Source [CC] Medium	(cases vs. controls) Race 60% vs. 60% White, 39.4% vs. 39.7% Other Age: <35 years 84.7% vs. 86.1% >35 years 15.3% vs. 13.9% SES: Education <12 years 44.8% vs. 41.9% 1>2 years 55.2% vs. 58.1% Income: <$20,000 33.9% vs. 32.0% > $20,000 66.1% vs. 68.0% Home situation: NR Unplanned pregnancy % Marital/partner status: NR Smoking% ETOH: 37% vs. 37% Substance abuse: NR	Mental health comorbidities NR Use of other psychoactive drugs NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits) Medical care environment (community/private/public clinic or hospital)	100% with diagnosis (exposed) Family history of depressive/mood disorders: NR Prior use of antidepressive drugs: NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Andrade, 2009[3] US Retrospective Cohort/Data Source [AD] Medium	Major: 1.51 (1.21-1.87)/0.69 (0.34-1.4)/1.18 (0.86-1.61)/1.25 (0.84-1.85)/1.41 (1.03-1.92)	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: Hospital	% with diagnosis NR Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Bakker 2010[4] CC/PBD Netherlands Medium	Race %: NR Mean Age: 30.3 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR	NR	NR
Bakker 2010[5] The Netherlands Case-Control Medium	Race: NR Mean Age: 31 SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR	NR	NR
Ban, 2012[6] U.K. PBD Medium	Race: NR Age: 15-17: 2.0%, 18-24: 21.4%, 25-34: 55%, 35-45: 21.6% SES: Townsend deprivation index score-1(least deprived): 22.8%, 2: 18.9%, 3:19.6%, 4: 19.0%, 5: 14.5% Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Maternal history of smoking: 40.6%	Provider characteristics: Primary care Other: NR	NR
Berard, 2007[7] Canada, Quebec LD Medium	Race %: NR Mean Age: 29.29 SES: Welfare Beneficiaries in years before pregnancy: 49.1% Home situation: Living alone in years before pregnancy: 69.3% Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: 52.1% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention):NR -Symptom severity:NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Bogen 2010/companion Wen 2009[8] U.S. PC	Race %: White/Other: 79.2%, African American: 20.8% Age:<31: 50.6%, ≥31: 49.4% SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: Married (or living as married): Yes:72.6%, No 27.4% Smoking%: 13.1%, ETOH: NR Substance abuse%: NR	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: Obstetrician, community worker	% with diagnosis: of MDD: 23%, % of patients with 1 episode of MDD: 30% Mean HDRS score: 13.28 (SD 4.4) Others: NR
Boucher, 2008[9] Canada LD Medium	Race: NR Mean Age: 29.5 SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking: 22.5% ETOH: 3% (occasional) Substance abuse: NR	Mental health comorbidities: NR Use of other psychoactive drugs: olanzapine (n=2), risperidone (n=2), alprazolam (n=3), bromazepam (n=1), clonazepam (n=7), lorazepam (n=4), Provider characteristics: NR Medical care environment: Secondary and tertiary care facilities hospital	NR
Casper 2003[10] US, California Cohort study Data/Source: [CC] Medium	Individual SSRIs: citalopram/escitalopram/fluoxetine/paroxetine/sertraline	Use of other psychoactive drugs: NR Provider characteristics: primary care and/or psychiatrist Medical care environment: public clinic	100% with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drugs: NR Symptom severity: (Likert scale, mean) exp vs. unexp: 1–3 months 4.2 (2.5) vs. 5.0 (2.5) 4–6 months 5.4 (3.2) vs. 5.0 (2.8) 7–9 months 6.1 (2.3) vs. 4.8 (3.0) Time of diagnosis: During pregnancy Diagnosis method: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Chambers, 1996[11] US, California CC Medium	Race %: NR Mean Age: 30.87 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: Exposed early group: 10%, Exposed late group: 17.8%, Controls, 3.8% ETOH: Exposed early group: 5.0%, Exposed late group: 1.5%, controls: 0.0% Substance abuse%: <1%	Mental health comorbidities % (e.g. anxiety): Anxiety 8.1%, panic disorder 6.4%, bipolar disorder 5.8%, obsessive-compulsive disorder 4.0% Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): benzodiazepine: 17.5%, trazodone: 5.2%, tricyclic 5.2% Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): hospital	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Chambers, 2006[12] US CC Medium	Race: 68.2% white, 11.8% black, 6% Asian, 11.2% Hispanic, 2.8% other Mean Age: <25: 25.3%, 25-30: 28.4%, 30-35: 30.8%, >35: 15.5% SES (education): <13 years: 29.8%, 13-15 years: 28.1%, >15 years: 42.1% Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking: Never: 59.3%, before pregnancy: 45.9%, during pregnancy: 16.7% ETOH: Never: 51.7%, before pregnancy: 23.9%, during pregnancy: 2.4% Substance abuse: NR	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: Neonatologists Medical care environment: NICU	NR
Cole 2007[13] US Case-control/Data Source[AD] Medium	Race NR Mean Age: 31 years SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking NR ETOH NR Substance abuse NR	Mental health comorbidities: (Monotherapy exposed vs. other Mono- or Poly therapy exposed vs. other) Bipolar disorder 1.0 vs. 0.7 vs. 1.0 vs. 0.8 Use of other psychoactive drugs: Carbamazepine: 0% vs. 0.2% vs. 0.1 vs. 0.2% Provider characteristics: physician Medical care environment: NR	% with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drug: Women received sertraline before pregnancy, but prescription did not overlap with the first trimester Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Cole, 2007[14] US LD Low	Age: 12-19: 1.5%, 20-24: 9.0%, 25-29: 28.1%, 30-34: 35.7%, 35-39: 20.4%, 40-49: 5.1% Other characteristics NR	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: NR	NR
Colvin 2012[15] PBD/CC Australia Medium	Race %: NR Mean Age: 30.05 SES: SEIFA = 997.1 Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR	NR	NR
Croen, 2011[16] US, California CC Medium	Race %: White, non-Hispanic: 47.8%; White, Hispanic: 19.2%; Black: 9.9%; Asian: 9.8%; Other: 13.3% Mean Age: 30.42 SES: Education: <high school: 6.9%; high school: 25.4%; college: 51.0%; postgraduate: 15.5%; Unknown: 1.2% Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety) Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia) Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits) Medical care environment (community/private/public clinic or hospital)	Depression Characteristics: -% with diagnosis -Family history of depressive/mood disorders (%) -Prior use of antidepressive drugs (%, for treatment or prevention) -Symptom severity -Time of diagnosis -Diagnosis method -When treatment commenced relative to the onset of symptoms
Davidson, 2009[17] Israel CC Medium	Race %: NR Mean Age: 29.71 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NSD between groups ETOH: 0% Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): hospital	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Davis, 2007[18] US LD Medium	Race %: NR Mean Age: NR SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking %: NR ETOH: NR Substance abuse %: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (pcp, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): hospital	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR --When treatment commenced relative to the onset of symptoms: NR
Dubnov-Raz, 2008[19] Israel CC Medium	Race %: NR Mean Age: NR SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): Excluded women treated with any other chronic medication Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): hospital	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Dubnov-Raz, 2012[20] Israel CC Medium	Race %: NR Mean Age: 33.2 years SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: 10% ETOH: 0% Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): Hospital	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
El Marroun 2012[21] Netherlands Prospective Cohort*Data Source [PC and PD] Low	Of the nervous system: 0.84 (0.21-3.37)/2.25 (0.32-16.05)/1.44 (0.36-5.79)/1.19 (0.17-8.45)/0.85 (0.12-6.07)	Mental health comorbidities % Anxiety Use of other psychoactive drugs: benzodiazepine %	7.4% with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drugs: N= 188 (excluded) Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Ferreira 2007[22] US Retrospective Cohort/Data Source[AD] Medium	Neural tube defects: Only fluoxetine=3.22 (0.45-23.03)	Mental health comorbidities: mixed disorders 26%, other anxiety disorders 16%, generalized anxiety disorders 3% Use of other psychoactive drugs: N=2 lithium .02% N=1 olanzapine .01% Provider characteristics NR Medical care environment: hospital	41 % with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Figueroa 2010[23] US Retrospective cohort Design/Data Source[AD] Medium	Of the eye: 2.62 (1.09-6.34)/None/0.93 (0.13-6.63)/None/1.05 (0.15-7.45)	Mental health comorbidities: Anxiety disorder N=1978 5.20% Adjustment disorder N= 1486 3.90% Other mental illness N=533 1.40% Bipolar disorder N=334 0.88% ADHD N=196 0.51% MR, PDD, or organic disorder N=168 0.44% Psychotic disorder N= 68 0.18% Use of other psychoactive drugs: Benzodiazepines during pregnancy N=311 0.82% Anticonvulsants during pregnancy N=147 0.39% Other psychotropics during pregnancy N=67 0.18% Provider characteristics: NR Medical care environment: mental health outpatient clinic	Depressive disorders N =3923 10.3% with diagnosis Anxiety disorder N=1978 5.20% Adjustment disorder N=1486 3.90% Other mental illness N= 533 1.40% Bipolar disorder N=334 .88% Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Gorman, 2012[24] US, California Prospective cohort/TIS Medium	Race %: 66% white, 20% Hispanic, 9% Asian, 5% Other Mean Age: 32.2 SES: Report any available values: 14% Low, 17% Medium, 69% High Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR	NR	NR
Grzeskowiak 2012[25] Australia Retrospective cohort/LD Medium	Race: 79% white, 9.6% Asian, 11% Other Mean Age: 29.2 Socioeconomic status (Socio-Economic Indexes for Areas, calculated from the Australian Bureau of Statistics'): 5 (highest)=20%, 4=20%, 3=18%, 2=20%, 1 (lowest)=22% Home situation NR Unplanned pregnancy NR Marital/partner status NR	Use of other psychoactive drugs: 1% anxiolytic use Provider characteristics NR Medical care environment NR	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Heikkinen, 2002[26] Finland PC	Race: NR Mean age: 32.6 SES: NR Home situation: NR Unplanned pregnancy: NR Marital status: NR % smoking: 23.8% ETOH %: light alcohol use: 9.5%	Mental health comorbidities % (e.g. anxiety):NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): 0% Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): Psychiatrists, pediatrician Medical care environment (community/private/public clinic or hospital):NR	% with depression: 28.6% Family history of depressive/ mood disorders: NR Prior use of antidepressive drugs: NR Symptom severity: NR Time of diagnosis: NR When treatment commenced relative to onset of symptoms: NR
Jimenez-Solem 2012[27] Denmark RC-PD Low	Race NR Age: <20-3%, 21-25=15%, 26-30=38%, 31-35=32%, >35=12% SES: Annual household income <$58,338=25%, $58335-$93-656=25%, $93,656-$119,082=25%, ≥ $119,082=25%; Education, short=33%, medium=30%, long=32% Home situation NR Unplanned pregnancy NR Marital/partner status NR Smoking: Daily cigarettes 0=78%, 1-10=15%, 11-20=0.6%, >20=2.4% ETOH NR Substance abuse NR	NR	NR
Jimenez-Solem, 2013[28] Denmark PBR Low	Race: NR Mean Age: <20: 2.9%; 21-25: 16.2%, 26-30: 38.4%, 31-35: 30.9%, >35: 11.6% SES: Education level low: 35.5%, medium: 32.5%, high: 31.8% Annual household income: <62,192: 24.9%, 62,192-89,140: 25.0%, 89,141-126,344: 25.0%, >126,344: 25.0% Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking (cigarettes/day): 0: 80.9%, 1-10: 12.8%, 11-20: 5.2%, >20: <1% ETOH: NR Substance abuse: NR	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: NR (stillbirth and neonatal mortality) Medical care environment: NR	NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Jordan 2008[29] US Clinic Appt Logs, Pediatrics records review AD Medium	W= .06%; AA 14%; Hisp 78%; Other .03% Mean Age: 27. Home Situation NR. Unplanned pg NR. Partner status NR	Mental Health comorbidities: Anx=12% in SRI pgs v. .06% non subjects; Adj DO 4% SRI gp/24% non SRI gp=15% all. BAD 4% SRI/12% non SRI = 0.8% all. Other drugs: Benzo (N=3). Med Care Envir: Hospital	% with Dx: NR Fam Hx NR; Prior use NR; Sx Severity NR; Dx method: NR; Tx/onset sxs: NR
Kallen, 2004[30] Sweden PBR Medium	Race %: NR Age: 13-19, 0.8%; 20-24, 10.8%; 25-29, 26.8%; 30-34, 34.4%; 35-39, 22.0%; 40-44, 4.9%; ≥45, 0.2% SES: NR Home situation: Cohabitating, 84.5% Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: 30.5% in early pregnancy ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): Anticonvulsants, 1.6%; Neuroleptics, sedatives, hypnotics, 18.7% Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Kallen 2007[31] Sweden Retrospective cohort/Data Source[PBR] Medium	Of the ear, face and neck: None/None/None/8.32 (1.16-59.81)/6.13 (0.85-44.05)	Mental health comorbidities %:NR Use of other psychoactive drugs: Clomipramine N=57 Trimipramine N= 2 Amitriptyline N=21 Nortriptyline N=4 Moclobemide N=3 Mianserin N=32 Nefazodone N=3 Mirtazapine N=27 Venlafaxine N=30 Reboxetine N=3 Provider characteristics NR Medical care environment NR	% with diagnosis: NR Family history of depressive/mood disorders: NR Prior use of antidepressive drugs NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Kallen 2008[32] Sweden Unclear/Data Source[PBR] Medium	Of the heart: 1.91 (1.31-2.77)/1.06 (0.34-3.3)/2.05 (1.27-3.31)/1.54 (0.77-3.1)/2.73 (1.75-4.26)	Mental health comorbidities % Use of other psychoactive drugs % Provider characteristics: NR Medical care environment: NR	% with diagnosis: NR Family history of depressive/mood disorders: NR Prior use of antidepressive drugs: NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Kieler 2012 [33] Nordic countries Retrospective cohort, PBD Medium	Age: ≤ 24=16.3%, 25-34=66.2%, 35-44=17.3%, ≥ 45=0.1% Others NR	NR	NR
Kornum, 2010 [34] Denmark PBR Medium	Race %: NR Mean Age: Median Age 29.8 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: With SSRI in first trimester or 30 days before conception: 35.8%, With SSRI in second or third month after conception: 31.8%, No SSRI: 20.6% ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): excluded women with both SSRI and non-SSRI antidepressants Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Laine 2003[35] Finland Prospective cohort/Data Source[PC] Medium	Race %: NR Mean Age: 32.5 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking: 60% vs 10% ETOH: 10% vs. 0% Substance abuse: NR	Mental health comorbidities: 50% panic disorder Use of other psychoactive drugs 3% benzodiazepines Provider characteristics: primary care physician Medical care environment: private/public clinic	50% with diagnosis N=10 Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Latendresse, 2011[36] U.S. PS Medium	Ethnicity: Hispanic 24%, Race: white: 69%, Hispanic/Mexican: 13%, African American, Other: 18% Mean age: NR SES: health insurance: private 56%, state Medicaid: 33%, Uninsured/self pay: 11% Home situation: NR Unplanned pregnancy: NR Marital status: married: 64%, living with partner: 13%, single: 21%, divorced/separated: 2% Smoking:<5%, ETOH:<5%, substance abuse:<5%	Anxiety: % NR Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: community	% with diagnosis: 1% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Lennestal, 2007[37] Sweden PBR Medium	Race %: NR Mean Age: NR; Age distribution: <20: 132, 20-24: 950, 25-29: 2032, 30-34: 2347, 35-39: 1426, 40-44: 306, ≥45: 19 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: 27.4% ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): Neuroleptics, sedatives, hypnotics: 21.2% of SNRI users Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Levinson-Castiel, 2006[38] Israel PC, PBD Medium	Race: NR Maternal Mean age: 31.8 years Socio-economic status: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR % Smoking: NR ETOH: NR Substance abuse %: NR	NR	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Lewis 2010 [39] Australia PC-Clinic Medium	Race NR Mean Age=32.3 years SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: Married=72%; de facto=22%; Widowed=5.6% Smoking: 15% ETOH: 48% Substance abuse: 5.6%	Mental health comorbidities NR Use of other psychoactive drugs: 41% medication other than antidepressants Provider characteristics: NR Medical care environment: NR	100% with diagnosis Family history of depressive/mood disorders NR Prior use of antidepressive drugs NR Symptom severity NR Time of diagnosis NR Diagnosis method: Independent psychiatric evaluation When treatment commenced relative to the onset of symptoms: NR
Logsdon, 2011[40] US, Pennsylvania PC Medium	Race %: White 79.5%, AA 18.1%, Other 2.3% Mean Age (SD): 30.4 (5.7) SES: Education level: high school or less 18.7%, Some college 16.4%, college 40.7%, graduate school 24.3%; Employment/academic status: Not at all 33.2%, Occasional 1.9%, Part time 10.3%, Full time 54.7%, Employed/attending school 66.8% Home situation: Partner, no children 30.2%, Partner and children 46.0%, Alone, no children 11.6%, Alone with children 9.3%, Parents, no children 0.5%, Parents and children 2.3% Unplanned pregnancy %: NR Marital/partner status: S 21.4%, Married/cohabitating 75.8%, Divorced/separated 2.3% Smoking %: NR ETOH: NR Substance abuse %: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): excluded women using benzodiazepines Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): Psychiatrist Medical care environment (community/private/public clinic or hospital): clinic	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Louik 2007[41] US CC	Race: NR Mean Age: NR SES: NR Home situation: NR Unplanned pregnancy %:NR Marital/partner status: NR Smoking%:NR ETOH:NR Substance abuse%:NR	None reported	None reported

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Lund, 2009[42] Denmark PC Medium	Race: NR Maternal age<20: 1.5%20-24:12.1%, 25-29:38.4%, 30-34:33.8%, ≥35:14.3% Nonsmoker: 78.4% Smoking cigarettes/day: 1-4:3.8%, 5-9:5.9%,10-14:5.9%, ≥15:3.2% Home situation: NR Unplanned pregnancy: NR Marital status Married/cohabiting: 89.9%, living alone: 2.9% ETOH (alcohol intake):<1:73.4%, 1-4:19.7%, 5-9:1%, ≥10:1.3% Education, years <9:15.8%, 9-12:26%, >12:37.5%	Mental health comorbidities Patients with psychiatric history but no use of SSRI group: schizophrenia: 0.2%, eating-disorder: 1%, bipolar disorder: 0.2%, OCD:0.4%, stress: 0.2%, anxiety: 0.5%, unspecified: 1.8% Use of other psychoactive drugs in SSRI use patients: benzodiazepines 2.4%, antipsychotics:4%, TCA: 3%, mirtazapine: 1.5%, venlafaxine:2.1%, sleeping pills: 0.6%, lithium: 0.3% Use of other psychoactive drugs in psychiatric history but no SSRI use patients: psychotropics: 0.5%, antipsychotics: 0.4%, anxiolytics: 0.3%, antidepressants other than SSRI: 0.7% Provider characteristics: GP, psychiatrist, psychologist Medical care environment: hospital	% with diagnosis reported in patients with psychiatric history but no SSRI: 1.8%
Malm, 2011[43] Finland TIS Low	Race %: NR Mean Age: Median Age 29.4 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: Married 60.20% Smoking%: 14.67% ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): 27.98% Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
McFarland, 2011 [44] US, Rhode Island PC Medium	Race %: Non White 13.04%, Hispanic 17.39% Mean Age: 29.1 SES: low SES 11.80% Home situation: NR Unplanned pregnancy %: NR Marital/partner status: Single 32.92% Smoking %: NR ETOH: NR Substance abuse %: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): obstetrician Medical care environment (community/private/public clinic or hospital): clinic	Depression Characteristics: -% with diagnosis: 40.37% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Merlob, 2009[45] Israel TIS Medium	Race %: NR Mean Age: Median Age NR SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): hospital	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Misri 2006[46] Canada PC-Clinic Medium	Race NR Mean Age: 32 years SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: 91% married, 9% common-law Smoking% ETOH: NR Substance abuse: NR	NR	NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Misri 2010[47] Canada PC-Clinic Medium	Race: 78% white, 0% AA, 0% Hispanic, 9% East Asian, 13% Other Mean Age: 32.5 years SES: Education=16.5 years Home situation: NR Unplanned pregnancy: NR Marital/partner status: 83% married, 15% common-law, 1% separated, 1% divorced Smoking NR ETOH NR Substance abuse NR	NR	NR
Mulder 2011[48] The Netherlands Prospective cohort/Data Source [PC] Medium	Race NR Mean Age: 31.5 (control vs. previously exposed vs. exposed) SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking:17.7% vs. 21.6% vs. 17.7% ETOH: 11.5% vs. 8.1% vs. 6.3% Substance abuse: NR	Mental health comorbidities Panic disorder: 9% Depression and panic combined: 46% Anxiety: 3% OCD: 1.5% Use of other psychoactive drugs % Provider characteristics: physician or mid wife Medical care environment: clinic	38 % with diagnosis N=133 Family history of depressive/mood disorders: NR Prior use of antidepressive drugs NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Nakhai-Pour, 2010[49] Canada CC Low	Race %: NR Mean Age: 27.52 SES: Recipients of social assistance: 30.90% Home situation: Urban Residences: 77.13% Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): Anxiety 6.79%, Bipolar 0.44% Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: 4.93% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Nordeng, 2012[50] Norway PBR Medium	Race: NR Mean Age: <20: 1.0%, 20-29: 44.2%, 30-39: 52.9%, >=40: 1.8% SES (education): primary: 3.0%, secondary: 35.4%, tertiary- short: 41.2%, tertiary- long: 20.3% Home situation: NR Unplanned pregnancy: NR Marital/partner status: Married/cohabiting: 96.5%, other: 3.5% Smoking: no: 89.9%, sometimes: 5.2%, daily: 5.0% ETOH: NR Substance abuse: NR	NR	Depressive symptoms at 17 gestational weeks: Nonexposed: 6.0% Prior-only: 22.1% Use of antidepressants during pregnancy: 39.9% Depressive symptoms at 30 gestational weeks: Nonexposed: 6.3% Prior-only: 22.1% Use of antidepressants during pregnancy: 38.4% Lifetime history of depression Nonexposed: 31.9% Prior-only: 86.8% Use of antidepressants during pregnancy: 88.7% Other characteristics NR
Nulman, 2002[51] Canada PC Medium	Mean Age: 31.2 Socioeconomic status (Score on Hollingshead index of social status): 44.1 Other characteristics NR	Mental health comorbidities: tricyclic antidepressants were taken for pain control in 11 cases and for an anxiety disorder in 3 cases. Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: NR	% with diagnosis: 100% Family history of depressive/mood disorders: NR Prior use of antidepressive drugs: NR Symptom severity (Mean [SD] Depression Score on CES-D Scale): 39.9 (11.3) fluoxetine, 28.0 (16.7) tricyclic antidepressants Duration of depression (Mean [SD]): 2.4 (0.5) years fluoxetine, 2.1 (1.0) years tricyclics Duration of treatment: (Mean [SD]): 1.9 (0.6) years fluoxetine, 1.8 (1.0) years tricyclics Time of diagnosis: NR Diagnosis method: Independent psychiatric evaluation

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Oberlander 2002[52] Canada Prospective cohort/Data Source[PC] Medium	Race NR Mean Age: NR SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking: NR ETOH: NR Substance abuse: NR	Mental health comorbidities NR Use of other psychoactive drugs: Clonazepam= 36% (N=14) Provider characteristics: NR Medical care environment: hospital	% with diagnosis NR Family history of depressive/mood disorders: NR Prior use of antidepressive drugs NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Oberlander, 2006[53] Canada, British Columbia PBR Medium	Race %: NR Mean Age: 29.51 SES: Drugs subsidized through welfare program in years before becoming pregnant 0.06%, Income decile: 5.6 Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): Diagnosed with mental health disorder, excluding depression, in years before becoming pregnant: 0.6% Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (pcp, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: 14.5% -Family history of depressive/mood disorders (%):NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Oberlander, 2008[54] Canada, British Columbia PC Medium	Race %: NR Mean Age: 32.32 SES: Maternal education: 16.46 years Home situation: NR Unplanned pregnancy % Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): Excluded all other psychotropic or antidepressant medications Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Oberlander, 2008[55] (Birth Defects Res Part B) Canada, British Columbia PBR Medium	Race %: NR Mean Age: 29 years SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): hospital	Depression Characteristics: -% with diagnosis -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Okun, 2011[56] US, Ohio and Pennsylvania PC Medium	Race %: White 78.7%, AA 17.6%, Other 3.8% Mean Age: 29.9 SES: Employed 59.4%, Education: Less than high school 7.1%, High school 11.3%, Some college 20.0%, College 37.5%, Graduate school 24.2% Home situation: NR Unplanned pregnancy %: NR Marital/partner status: S 24.2%, Married/cohabitating 72.1%, Divorced/separated 3.3%, Widowed 0.4% Smoking%: 14.7% ETOH: 32.6% Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): community	Depression Characteristics: -% with diagnosis: 24.6% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Okun, 2012[57] US, Ohio and Pennsylvania PC Medium	Race %: White, 77.9% Mean Age: 30.1 SES: Employed, 59.3%; Education level: < high school 7.4%, high school 10.6%, some college 18.4%, college 40.1%, graduate school 23.5% Home situation: NR Unplanned pregnancy %: NR Marital/partner status: Married/Cohabitating 72.8% Smoking%: Ever during pregnancy 13.0%; No. cigarettes per day: 4.9±0.9 ETOH: Ever during pregnancy 30.8%; No. drinks per occasion: 2.3±2.1 Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (pcp, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: 24.44% -Family history of depressive/mood disorders (%):NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Palmsten 2012[58] Canada RC-LD Medium	Race NR Median Age=30 years SES NR Home situation NR Unplanned pregnancy NR Marital/partner status NR Smoking NR ETOH NR Substance abuse NR	Mental health comorbidities: % with other mental health disorder=3.9% Use of other psychoactive drugs: 0.93% anticonvulsant dispensing; 0.76% antipsychotic dispensing; 8.4% Provider characteristics: NR Medical care environment: NR	100% with diagnosis Family history of depressive/mood disorders NR Prior use of antidepressive drugs: Total antidepressant days' supply in the years before the LMP=265; number of antidepressant classes used in the years before the LMP, 0=12%, 1=75%, 2=14%, 3-4=2% Symptom severity NR Time of diagnosis NR Diagnosis method NR When treatment commenced relative to the onset of symptoms NR
Pearson 2007[59] US, Louisiana Retrospective cohort Data/Source: [AD] Medium	Race NR Mean Age: 33 vs. 33 SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: 97% vs. 77% Married Smoking 24% vs. 54% ETOH NR Substance abuse: NR	Mental health comorbidities % 36% panic disorder 5% OCD 5% other anxiety disorders Use of other psychoactive drugs: 28.6% benzodiazepine (exposed) Provider characteristics: psychiatrist Medical care environment: hospital	53.4% with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR
Pedersen, 2009[60] Denmark PBD, LD Medium	"Women taking an SSRI were more likely to be older, living alone, unmarried and smokers." Data not shown. Others NR	Mental health comorbidities: NR Use of other psychotropic drugs: 1.2% for women with no recorded use of antidepressants, 16% in SSRI group use of TCA: n=42 (0.008%, Venlafaxine: n=91, 0.02%)	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Pedersen, 2010[61] Denmark PC Medium	Race %: NR Mean Age: 29.81% SES: Education level: High: 55.75%, Middle: 34.07%, Low: 9.29% Home situation: Live with partner: 94.47%, Live alone: 5.53% Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: 47.35% ETOH: 40.60% Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): excluded women taking psychotropic medications other than antidepressants Provider characteristics (pcp, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Rai 2013[62] Sweden CC Low	Race NR Mean Age: 29.5 years SES: Family income highest 5th=21%, lowest 5th=16%; parental education > 12 years=49%, 10-12 years=48%, <9 years=7.3%; occupational class: higher professionals=19%, intermediate non-manual employees=20%, lower non-manual employees=15%, skilled manual workers=14%, unskilled manual workers=14%, self-employed=4.8%, unclassified=12% Home situation NR Unplanned pregnancy NR Marital/partner status NR Smoking NR ETOH NR Substance abuse NR	Mental health comorbidities: Anxiety disorder=6.2%, psychotic disorder=3.5%, other psychotic disorder=1.1% Use of other psychoactive drugs NR Provider characteristics NR Medical care environment NR	0.06% with diagnosis Family history of depressive/mood disorders NR Prior use of antidepressive drugs NR Symptom severity NR Time of diagnosis NR Diagnosis method NR When treatment commenced relative to the onset of symptoms NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Ramos, 2008[63] Canada, Quebec LD Medium	Race %: Questionnaire subgroup, N=806; White: 87.3%, Black: 1.9%, Other: 10.8% Mean Age: 28.3 SES: Welfare Recipient, 46.2% Home situation: Living alone, 29.8% Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: Questionnaire subgroup, 34.2% ETOH: Questionnaire subgroup, 19.7% Substance abuse%: Questionnaire subgroup, illicit drug use 6.82%	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): At least one anxiolytic/sedative prescription: 18.8% Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: 25% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Ramos, 2010[64] Canada, Quebec LD, supplemental questionnaire Medium	Race %: NR Mean Age: 27.84 SES: Welfare recipient: 49.1%; Education Level >12y: 33.7% Home situation: Living Alone: 27.8% Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH:NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): Number of different psychiatric disorder diagnoses: ≤2: 59.9%, 3-5: 31.2%, >5: 8.9% Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): ≥1 anxiolytic or sedative prescription: 18.5%; ≥1 anticonvulsive prescription: 13.1% Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Rampono, 2009[65] Australia PC Medium	Race: NR Median Age (range): 31 (24-37) SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking (during pregnancy): 11% ETOH (during pregnancy): 19.8% Substance abuse: Known substance abusers were excluded	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: Outpatient clinics	NR
Reebye, 2002[66] Canada PC Medium	White: 88.5%, Asian: 9.8%, Other: 1.6% Mean age: 31.8 years M: 93.4%, S or D: 3.3% SES: NR Home situation: NR Unplanned pregnancy %: NR	Provider characteristics: Psychiatrist 14 patients taking SSRI + benzodiazepine Mental health comorbidity: NR	NR
Reis, 2010[67] Sweden PBR Medium	Race: NR Age: <20: 2%,20-24: 12%, 25-29: 27%, 30-34: 34%, 35-39: 20%, 40-44: 4.6%, >=45:0.2 % SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: 2% unknown, 85% co-habiting, 6% living alone, 6% other Smoking: 2% unknown, 74% no, 14% <10 cigarettes/day, 9% >=10 cigarettes/day ETOH: NR Substance abuse: NR	Mental health comorbidities: NR Use of other psychoactive drugs: 11% sedatives or hypnotics Provider characteristics: NR Medical care environment: NR	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Salisbury, 2011[68] US, Rhode Island PC Medium	Race %: Hispanic 12.73%, Non-white 14.55% Mean Age: 29.3 SES: low SES 9.82% Home situation: NR Unplanned pregnancy %: NR Marital/partner status: not married: 34.23% Smoking%: 18.35% ETOH: 46.79% Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (pcp, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): Hospital	Depression Characteristics: -% with diagnosis: 50% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: 8.0 -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Salkeld 2008[69] Canada CC-LD Low	Race: NR Mean Age=26 years SES NR Home situation NR Unplanned pregnancy NR Marital/partner status: NR Smoking NR ETOH NR Substance abuse NR	NR	NR
Simon 2002[70] U.S. RC-HCDB Low	NR	Mental health comorbidities NR Use of other psychoactive drugs NR Provider characteristics NR Medical care environment: Primary care facilities owned by Group Health Cooperative	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Sit, 2011[71] US, Pennsylvania PC Medium	Race %: NR Mean Age: 31 SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: 23.8% ETOH: excluded women with alcohol abuse Substance abuse%: excluded women with substance abuse	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): Psychiatrist Medical care environment (community/private/public clinic or hospital): Clinic	Depression Characteristics: -% with diagnosis: 100% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: Structured Interview Guide for HAM-D Atypical Depression Symptoms, Mean=16.0±7.6 -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR
Stephansson, 2013[72] Sweden PBR Medium	Race: NR Mean Age: <=24: 16.3%, 25-34: 66.2%, 35-44: 17.4%, >=45: 0.1% SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking in early pregnancy: 78.1% no, 15.6% yes, 6.3% missing data ETOH: NR Substance abuse: NR	Mental health comorbidities: 3.9% had a previous psychiatric hospitalization Use of other psychoactive drugs: NR Provider characteristics: NR (stillbirth and neonatal mortality) Medical care environment: NR	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Suri, 2007[73] US, California PC Medium	Race %: NR Mean Age: 33.8y SES: College degree 87% Home situation: NR Unplanned pregnancy %: NR Marital/partner status: Married 90% Smoking%: 2.2% ETOH: 2.2% Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): obstetrics, psychiatric Medical care environment (community/private/public clinic or hospital): clinic Depression Characteristics: -% with diagnosis: 78.5% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: HAM-D: Maximum 21 -item score M=17.2, Maximum 28-item score M=23.5; Maximum Beck Depression Inventory score M=9.8; Maximum Perceived Stress Scale M=9.3 -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR	Depression Characteristics: -% with diagnosis: 78.5% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: HAM-D: Maximum 21 -item score M=17.2, Maximum 28-item score M=23.5; Maximum Beck Depression Inventory score M=9.8; Maximum Perceived Stress Scale M=9.3 -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Suri, 2011[74] US, California PC Medium	Race %: NR Mean Age: 334.84% SES: Education, M=17.57y Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%: NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): clinic	Depression Characteristics: -% with diagnosis: lifetime diagnosis 76.6% -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: Hamilton Depression Rating Scale, M=9
Toh, 2009[75] US CC Medium	Race: 72.6% white, 6.9% black, 13.2 % Hispanic, 7.3% other Mean Age: <25: 18.9%, 25-29: 23.2%, 30-34: 35.5%, >=35: 21.9% Socioeconomic status: Education (years): <=12: 26.7%, 13-15: 24.1%, >15: 49.2% Home situation: NR Unplanned pregnancy: NR Married or living with child's partner: 89.7% Smoking during pregnancy: Never: 59.1%, past smoker: 25.5%, <10 per day: 7.9%, >=10 per day: 8.5% ETOH during pregnancy: Never: 45.7%, past drinker: 50.3%, drank: 3.3% Substance abuse: NR	Mental health comorbidities: NR Use of other psychoactive drugs: 0.8% Provider characteristics: NR Medical care environment: Various (hospitals, clinics, PICUs)	NR
Ververs, 2009[76] the Netherlands AD Medium	Race %: NR Mean Age: 30.3 years SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: NR Smoking%: NR ETOH: NR Substance abuse%:NR	Mental health comorbidities % (e.g. anxiety): NR Use of other psychoactive drugs % (antipsychotics, antianxiety agents (e.g., benzodiazepines), and drugs for insomnia): NR Provider characteristics (primary care physician, obstetrician, psychiatrist, nurse, midwife, community worker, or pediatrician visits): NR Medical care environment (community/private/public clinic or hospital): NR	Depression Characteristics: -% with diagnosis: NR -Family history of depressive/mood disorders (%): NR -Prior use of antidepressive drugs (%, for treatment or prevention): NR -Symptom severity: NR -Time of diagnosis: NR -Diagnosis method: NR -When treatment commenced relative to the onset of symptoms: NR

	Population Characteristics		
Author Year Country Study Design/Data Source Risk of Bias	**1. Race % Mean Age Socioeconomic Status Home Situation Unplanned Pregnancy % Marital/Partner Status Smoking % ETOH Substance Abuse %**	**2. Mental Health Comorbidities % Use of Other Psychoactive Drugs % Provider Characteristics Medical Care Environment**	**3. Depression Characteristics: - Percent with Diagnosis - Family History of Depressive/Mood Disorders (%) - Prior Use of Antidepressive Drugs (%, for Treatment or Prevention) - Symptom Severity - Time of Diagnosis - Diagnosis Method - When Treatment Commenced Relative to the Onset of Symptoms**
Wen 2006[77] Canada RC, PBD Medium	Race: NR Age: <19: 7.6%, 20-29: 55.3%, ≥30: 37.1% Social assistance: 14.6% Home situation: NR Unplanned pregnancy: NR Smoking %: NR ETOH: NR Substance abuse: 0.7%	NR	NR
Wilson, 2011[78] US CC Medium	Race: NR Advanced maternal age (>=35): 10% SES: NR Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking (tobacco use yes): 7.1% ETOH: NR Substance abuse: NR	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: Army Medical Center	NR
Wisner, 2009[79] US, Ohio Prospective cohort Medium	Race: 67% white, 12% AA, 2% Other Mean Age: 39% < 31 years, 41% > 31 years SES: NR Home situation: NR Unplanned pregnancy %: NR Marital/partner status: 64% Married/partner	NR	% with diagnosis: 100% Family history of depressive/mood disorders (%): NR Prior use of antidepressive drugs (%, for treatment or prevention): NR Symptom severity: HAM-D 17: 4.9 (range across groups 4.2 - 14.9). Time of diagnosis: baseline Diagnosis method: HAM-D 17, Structured Interview Guide for the Hamilton Depression Rating Scale With Atypical Depression Supplement, GAS, SF-12 Mental Component When treatment commenced relative to the onset of symptoms: NR
Wogelius, 2006[80] Denmark PBR Medium	Age: <25: 13%, 25-30: 46%, >30: 42.1% Smoking: 24.2% smokers Other characteristics NR	Mental health comorbidities: NR Use of other psychoactive drugs: NR Provider characteristics: NR Medical care environment: NR	NR

	Population Characteristics		
Author **Year** **Country** **Study Design/Data Source** **Risk of Bias**	**1. Race %** **Mean Age** **Socioeconomic Status** **Home Situation** **Unplanned Pregnancy %** **Marital/Partner Status** **Smoking %** **ETOH** **Substance Abuse %**	**2. Mental Health Comorbidities %** **Use of Other Psychoactive Drugs %** **Provider Characteristics** **Medical Care Environment**	**3. Depression Characteristics:** **- Percent with Diagnosis** **- Family History of Depressive/Mood Disorders (%)** **- Prior Use of Antidepressive Drugs (%, for Treatment or Prevention)** **- Symptom Severity** **- Time of Diagnosis** **- Diagnosis Method** **- When Treatment Commenced Relative to the Onset of Symptoms**
Yonkers 2012[81] US Prospective Cohort [PC] Low	Race 74% White 7% Black 14% Hispanic,5% Other Mean Age: 31 SES: Education (years) <12, 6% 12, 14% 13-15, 23% 16+, 57% Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking 15% ETOH NR Substance abuse 8%	Mental health comorbidities % PDSD 5% Anxiety 10% Panic disorder 4% Use of other psychoactive drugs % Provider characteristics: obstetrician:clinic or hospital	100% with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: DSM-IV and screened positive for depressive episode and antidepressant treatment.
Zeskind 2004[82] US Prospective cohort study/Data Source [PC, AD] Medium	Race: 94% white Mean Age: 33 years (1.36) Low socio economic status: N=3 Home situation: NR Unplanned pregnancy: NR Marital/partner status: NR Smoking% ETOH: 70% Substance abuse 2%	Mental health comorbidities NR Use of other psychoactive drugs NR Provider characteristics NR Medical care environment NR	100% with diagnosis Family history of depressive/mood disorders: NR Prior use of antidepressive drugs (%, for treatment or prevention) NR Symptom severity: NR Time of diagnosis: NR Diagnosis method: NR

Author, year Country Study Design/Data Source Risk of Bias	4. Exposures (N, duration, dose) Controls (N)	5. Exposure Period	6. Confounders
Alwan 2007[1] US Arm of Case Control Studied, Population based Medium	Fluoxetine, Sertraline, Paroxetine. Duration: 1 month before pg-3 month after conception	1 month before pg - 3 month after conception	Maternal race, obesity, maternal smoking, family income
Alwan 2010[2] Canada Case-control/Data Source[CC] Medium	Bupropion N = 90 Cases: N=64 Controls: N=26 Duration NR Unexposed N = 17353 Cases: N=11,733 Controls: N=5626	Between 1 month before and 3 months after conception.	Adjusted for maternal age, maternal race, maternal education, maternal obesity before pregnancy (body mass index 30 kg/m2, 30 kg/m2), maternal smoking and alcohol use from1 month before to 3 months after conception, use of a dietary supplement containing folic acid from 1 month before to 1 month after conception, annual family income plurality ,and parity.
Andrade, 2009[3] US Retrospective Cohort/Data Source [AD] Medium	Average daily doses of sertraline, fluoxetine, and paroxetine were 113.2 ± 72.3 mg, 20 ± 11.9 mg, and 17.2 ± 10.1 mg	Third trimester exposure	None adjusted for (Data NA)
Bakker 2010[4] CC/PBD Netherlands Medium	Paroxetine (N = 6, T1) Controls (N=605)	T1	Year of birth
Bakker 2010[5] The Netherlands Case-Control Medium	Exposure=Paroxetine; dose and duration NR Cases N=678 Controls N=615	First trimester: Any use from 4 weeks before conception through the 12th week of pregnancy	Adjusted for year of birth, pregnancy outcome, maternal age, gravidity, mother's educational level, smoking, use of alcohol, BMI, folic acid use, and pre-existing maternal diabetes or epilepsy
Ban, 2012[6] U.K. PBD Medium	N= all pregnancies Exposure TCA: N=3019 SSRI:N= 10312 Control: No history N= 390665, unmedicated mental illness: N= 3647	First trimester	Maternal age at the end of pregnancy, most recent recording of smoking status before delivery, BMI before pregnancy and quintiles of Townsend's Index of Deprivation for each woman's postcode of residence, no. of previous known live births for each pregnancy

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Berard, 2007[7] Canada, Quebec LD Medium	Paroxetine (N=542) Dose, M=22.4mg±9.0 Duration, M=64d±2.3 Other SSRI (N=443) Dose, Duration, NR Sertraline, n=186 Citalopram, n=113 Fluoxetine, n=101 Fluvoxamine, n=43 Non-SSRI antidepressants (Control Group) (N=293) Dose, Duration, NR Venlafaxine, n=153 Amitriptyline, n=140	First trimester: 0-14 weeks of GA	Adjusted for antidepressant exposure during the second and third trimesters, GA, maternal age, mean number of prenatal visits, visits to an obstetrician during pregnancy, pregnancy in the year before this pregnancy, diagnosis of diabetes, hypertension and depression in the year before or during pregnancy, place of residence, living alone, welfare status, calendar year, mean number of physician visits in year before pregnancy, number of different medications excluding antidepressants, number of different prescribers in year before and during pregnancy.
Bogen 2010/companion Wen 2009[8] U.S. PC	Physically healthy but taking antidepressant during pregnancy for MDD , n=38 (SSRI), n=4 SRI, n=1 (bupropion), duration: N MDD during pregnancy but no gestational antidepressant exposure, N=NR No current psychiatric disorder and no antidepressant, N=NR	Pregnancy to 2 years postpartum	Women's prior breast feeding experience, maternal age, race, marital statu, smoking, maternal obesity, SRI use
Boucher, 2008[9] Canada LD Medium	Exposed: N=73 (22 citalopram, 19 paroxetine, 10 sertraline, 4 fluoxetine, 2 fluvoxamine, 12 venlafaxine, 3 amitriptyline, 3 trazodone, 1 mirtazapine) Duration NR Controls: N=73	Late pregnancy (last 3 weeks of pregnancy)	Gestational age at birth, maternal age and other medications taken by the mother.
Casper 2003[10] US, California Cohort study Data/Source: [CC] Medium	Any SSRI, N = 31 23% fluoxetine, 26%paroxetine, 3.2% fluvoxamine Duration: Throughout: N=13 First trimester: N=22 Third trimester: N=23 Dose: average daily doses sertraline 113.2 ± 72.3 mg, fluoxetine 20 ± 11.9 mg, paroxetine 17.2 ± 10.1 mg Control: Unexposed N = 13	71% before or during pregnancy 45% throughout 71% first trimester 74% third trimester 29% after delivery	Adjusted for age at delivery, marital status, years of schooling, parity, weight gain, and self-rated levels of depression

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Chambers, 1996[11] US, California CC Medium	Controls (N=223) Fluoxetine, N=173 Dose M= 26.73 Duration: NR	At study entry, through: Exposed Early group: 93% discontinued in first trimester 7% first and second trimester Exposed Late group: 82.2% first, second third trimester 9.6% second and third trimester 5.5% third trimester only 2.7% first and third trimester only	Adjusted for multiparity, previous spontaneous abortion, preeclampsia, eclampsia, hypertension, smoking status, maternal age, SES, race, average dose of fluoxetine, gestational diabetes, use of other psychotherapeutic drugs, alcohol use, evidence of maternal age, SES, race, average dose of fluoxetine, gestational diabetes, use of other psychotherapeutic drugs, alcohol use, evidence of maternal or neonatal infection near delivery, prematurity, mode of delivery.
Chambers, 2006[12] US CC Medium	Cases N= 377 (16 SSRI, 4 other antidepressant) Controls: N= 836 (24 SSRI, 13 other antidepressant) Duration NR	Before week 20 (n=32) After week 20 (n=25)	Single or multiple pregnancy, maternal diabetes, maternal smoking, maternal alcohol use, maternal NSAID use after week 20.
Cole 2007[13] US Case-control/Data Source[AD] Low	Paroxetine vs. other antidepressants* Monotherapy N = 791 Mono or Polytherapy: N=989 Other antidepressants: Monotherapy N = 4072 Mono or Poly therapy: N=4767 Duration NR Control: Exposed to other antidepressants N = 4767 (mono or poly) and 4072 (monotherapy) * including selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors,serotonin-2 antagonist reuptake inhibitors, tricyclics, and monoamine oxidase inhibitors)	First trimester.	Adjusted for all of the covariates derived from the medical and pharmacy claims data and indicators for paroxetine exposure, maternal age category, geographic region of the health plan, and infant sex.
Cole, 2007[14] US LD Medium	Exposed: N=1213 bupropion, 4743 other antidepressant Controls: N=1049 (bupropion outside first trimester)	1st trimester	Diagnoses of bipolar disorder and eclampsia within 1 year before delivery, dispensing of lithium, phenytoin, and fluconazole within 1 year before delivery through the end of the 1st trimester, and the number of physician visits within 10-12 months before delivery; maternal age, geographic region of the health plan, and infant sex.

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Colvin 2012[15] PBD/CC Australia Medium	Any SSRI: citalopram, paroxetine, sertraline, fluoxetine, escitalopram, fluvoxamine (N=3764, varies) Controls (N=94,561)	T1:Trimester 1 T2 or T3: Trimester 2 or 3 only Any: Any time during pregnancy	Preterm birth (<37 Weeks) was adjusted for previous preterm birth, smoked during pregnancy, SEIFA, parity, maternal age; singletons only Birth weight (<2500g) was adjusted for gestational age, smoking during pregnancy, SEIFA, sex, parity, maternal height; singletons only
Croen, 2011[16] US, California CC Medium	SSRIs (N=49) citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline Dual-action antidepressants (N=10) nefazodone, trazodone, venlafaxine, serotonin-noradrenergic-reuptake inhibitors, noradrenergic and specific serotoninergic antidepressants, and noradrenaline-reuptake inhibitors Tricyclic antidepressants (N=22) amitriptyline, desipramine, doxepin, imipramine, nortriptyline, protriptyline SSRIs only, N=38 SSRIs + tricyclic antidepressants or dual-action antidepressants, N=11	Preconception: 3 months prior to LMP First trimester: first 90 days after LMP Second trimester: 91-180 days after LMP Third trimester; 181 days after LMP to date of delivery	Adjusted for age, race/ethnicity, education of mother, birth weight, sex, birth year, birth facility
Davidson, 2009[17] Israel CC Medium	Controls (N=20) Paroxetine (N=8) Fluoxetine (N=7) Citalopram (N=6)	Entire pregnancy	Groups matched for gestational age. Excluded from study: Diabetes, chronic hypertension, CV disease.
Davis, 2007[18] US LD Medium	Assessing congenital anomalies: Tricyclic Antidepressants (N=221) SSRIs (N=1047) Other antidepressants (N=173) Non-exposed (N=49,663) Assessing perinatal complications: Tricyclic Antidepressants (N=339) SSRIs (N=1602) Other antidepressants (N=260) Nonexposed (N=75,833)	Assessing congenital anomalies: First trimester exposure Assessing perinatal complications: Third trimester exposure	Unadjusted
Dubnov-Raz, 2008[19] Israel CC Medium	Controls (N=52) Paroxetine (N=25), Citalopram (N=13), Fluoxetine (N=12), Fluvoxamine (N=1), Venlafaxine (N=1), duration and doses NR	NR, women were taking SSRI at onset of labor	Excluded gestational diabetes and hypothyroidism

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Dubnov-Raz, 2012[20] Israel CC Medium	SSRI (N=40); High dose: fluoxetine, citalopram ≥ 40mg/day, escitalopram ≥20mg/day ; Duration: 92.5% throughout entire pregnancy Controls (N=40)	Throughout pregnancy	Adjusted for maternal age, maternal smoking status, previous births, GA, infant sex, birth weight z-score, birth length
El Marroun 2012[21] Netherlands Prospective Cohort*Data Source [PC and PD] Low	SSRIs during pregnancy N=99,1.3% Duration NR Control: Unexposed (with low depressive symptoms) N=7027, 91.3%	First trimester only, N=47 First trimester plus 1 additional trimester, N=52	Adjusted for BMI, educational level, maternal smoking habits, maternal age, ethnicity, fetal sex, parity, and maternal use of benzodiazepines, but not maternal drinking habits and cannabis. For effects of depressive symptoms and SSRI use on head growth also adjusted for fetal body size measures.
Ferreira 2007[22] US Retrospective Cohort/Data Source[AD] Medium	Exposed to SSRIs or venlafaxine: N=76 46 (60.5%) paroxetine (5–40 mg) 10 (13.2%) fluoxetine (10–40 mg) 9 (11.8%) venlafaxine (75–150 mg) 6 (8%) citalopram (10–30 mg), 3 (3.9%) sertraline (125–150 mg), 2 (2.6%) fluvoxamine (50–150 mg) Mean duration SSRIs: 32 months (range: 1–132 months) Controls: Unexposed N= 90	Third trimester or at least two weeks prior to delivery	Adjusted for prematurity, maternal age 35 years, smoking, illicit drug use, cesarean section, maternal hypertension, prolonged preterm rupture of membranes, history of prematurity, history of 2 miscarriages, gestational diabetes, and small for gestational age.

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Figueroa 2010[23] US Retrospective cohort Design/Data Source[AD] Medium	SSRI before pregnancy N=954 2.51% SSRI during pregnancy N=916 2.41% First trimester N=564 1.48% Second trimester N=450 1.18% Third trimester N=564 1.48% SSRI after pregnancy N=1,948 5.12% Bupropion before pregnancy N=165 0.43% Bupropion during pregnancy N=114 0.30% First trimester N=79 0.21 % Second trimester N=46 0.12% Third trimester N=7 0.10% Bupropion after pregnancy N=185 0.49% Other antidepressant during pregnancy N=119 0.31% Dose: NR Controls: Unexposed N=168	Before pregnancy First trimester Second trimester Third trimester Throughout	Adjusted for maternal and paternal mental health diagnoses, presence or absence of maternal mental health-related visits by period of time (year of child's life), use of other psychotropics during pregnancy, and perinatal complications.
Gorman, 2012[24] US, California Prospective cohort/TIS Medium	Any SSRI Exposure before delivery: 117 Exposures at delivery: 197 Unexposed: 182	Means: Exposed early: 12 weeks Exposed at deliver: 33 weeks	Maternal age, SES category, and race/ethnicity, maternal characteristics, reproductive history, (any alcohol use in pregnancy, cesarean birth, and low 5-minute Apgar scores and birth characteristics
Grzeskowiak 2012[25] Australia Retrospective cohort/LD Medium	SSRI use N=221 Psychiatric illness/no SSRI use N=1566 No psychiatric illness N=32,004	Late gestation=Definition NR	Preterm delivery adjusted for maternal age, socioeconomic status, smoking status, race, asthma, preexisting diabetes, alcohol abuse, substance abuse, hypertension, parity, epilepsy, thyroid disorder, previous history of premature delivery, and anxiolytic use Low birth weight adjusted for same as preterm delivery plus maternal H4-SGA, neonate admitted to hospital, neonate length of hospital stay > 3 days adjusted for maternal age, socioeconomic status, smoking status, race, asthma, preexisting diabetes, alcohol abuse, substance abuse, hypertension, parity, epilepsy, thyroid disorder, and anxiolytic use.
Heikkinen, 2002[26] Finland PC	Exposure: Citalopram 20-40mg QD, n=11, duration: NR Controls: n=10	During pregnancy up to 1 year	age, gravidity, parity, time and mode of delivery

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Jimenez-Solem 2012[27] Denmark RC-PD Low	Any SSRI, dose and duration NR First trimester exposure N=4183 Paused during pregnancy N=806 Unexposed N=843,797	First trimester: Between ≥1 month before conception and day 84 Paused exposure: No exposure between 3 months before conception and 1 month after giving birth	Adjusted for mother's age, parity, income, education, smoking and year of conception. SSRI, selective serotonin reuptake inhibitor
Jimenez-Solem, 2013[28] Denmark PBR Low	Exposed: N=6,378 (2,434 fluoxetine, 1,800 citalopram, 212 escitalopram, 734 paroxetine, 1,654 sertraline) Unexposed: N=908,214	1st trimester (n=3982) 1st and 2nd trimesters (n=2065) All trimesters: (n=6,378)	Smoking, birth year, prior stillbirths, mother's age, annual household income, education level, parity,
Jordan 2008 [29] US Clinic Appt Logs, Pediatrics records review AD Medium	SRI Any N=49. Duration NR; controls= unexposed AND discontinued last month of pregnancy	NR	Analyzed 3 pregnancies with benzodiazepines separately
Kallen, 2004[30] Sweden PBR Medium	SSRI (N=558): Citalopram, n=285 Paroxetine, n=106 Fluoxetine, n=91 Sertraline, n=77 Other antidepressants (N=63) Venlafaxine, n=24	Throughout pregnancy; weeks of pregnancy NR, n=387 drug stopped before week 24, n=70 drug started or continued past week 23, n=561	Adjusted for year of birth, maternal age, parity, and maternal smoking in early pregnancy
Kallen 2007[31] Sweden Retrospective cohort/Data Source[PBR] Medium	Exposed SSRIs N = 6,481, 96.5% only one SSRI Fluoxetine N=860 Citalopram N=2,579 Paroxetine N=908 Sertraline N=1,807 Fluvoxamine N=36 Escitalopram N= 66 Duration: NR Dose: NR	First trimester	Adjusted for maternal age, parity, smoking, previous miscarriage, BMI, years of subfertility and maternal country of birth.

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Kallen 2008[32] Sweden Unclear/Data Source[PBR] Medium	Exposed: N= 7587 SSRIs: 39% Citalopram 31% Sertraline 15% Fluoxetine 13% Paroxetine 2% Fluvoxamine or escitalopram Dose: NR Controls: All other registered births N= 831,324 Other: Mirtazapine N=1	First trimester, some late exposure	Adjusted for maternal age, parity, BMI, and smoking.
Kieler 2012[33] Nordic countries Retrospective cohort, PBD Medium	Any SSRI, fluoxetine, citalopram, paroxetine, sertraline, or escitalopram N = 2145 Duration NR Control: Unexposed N = 2300	Ever: 3 months before pregnancy until birth Early: 3 months before pregnancy until pregnancy length of 55 days Late: From 140 days after the start of pregnancy until birth	Adjusted for maternal age, dispensed non-steroidal anti-inflammatory drugs and anti diabetes drugs, pre-eclampsia, chronic diseases during pregnancy, country of birth, birth year, level of delivery hospital and birth order
Kornum, 2010[34] Denmark PBR Medium	No SSRI (N= 213,049) Any SSRI (N= 2,993, duration and dose NR)	Early: From 30 days prior to conception to the end of the first trimester Second/Third month.: During the second or third month of pregnancy	Excluded from study: Antiepileptics within 90 days prior to conception or during first trimester Antidiabetic drugs at any time prior to conception or during pregnancy ORs adjusted for maternal smoking status, maternal age, birth order and birth year.
Laine 2003[35] Finland Prospective cohort/Data Source[PC] Medium	SSRIs: Citalopram, Fluoxetine N = 20 Duration: exposure during pregnancy ranged from 7- 41 weeks Dose: mean (range) Citalopram: 20mg (20-40) Fluoxetine: 20mg (20-40) Control: Unexposed N = 20	During pregnancy and lactation	Adjustment NR Controls matched age, gravidity, parity, duration of pregnancy and time and mode of delivery.

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Latendresse, 2011[36] U.S. PS Medium	Total N: exposed and non exposed: 100 SSRI: n, dose and duration: NR Control: Unexposed patients, n, dose, duration NR	NR	Pregnancy related anxiety, corticotropin releasing hormone and SSRI use for depression and anxiety, age, antepartum complications (including previous history of Pre-term birth
Lennestal, 2007[37] Sweden PBR Medium	SNRI Use (N=732) Mianserin, n=61 Mirtazapine, n=144 Venlafaxine, n=501 Reboxetine, n=14 Venlafaxine + mirtazapine, n=9 Venlafaxine + mianserin or reboxetine, n=3 SSRI Use comparison group (N=6481) No. women in register, controls (N=860,215) Doses, durations NR	Throughout pregnancy; "Early" exposure: maternal use of the drug prior to first antenatal care visit (usually near end of first trimester) "Late" exposure: maternal use of the drug after the "early" exposure period.	Adjusted for year of delivery, maternal age, parity, and smoking in early pregnancy, BMI class
Levinson-Castiel, 2006[38] Israel PC, PBD Medium	SSRIs (n=60)N, dose range: paroxetine:37, 10-40mg; fluoxetine:12, 20-60mg; citalopram: 8,10-40mg; venlafaxine:2, 37.5-75mg Duration, mean, SD, wks: 35.5 (8.7) Control-non-SSRI exposed neonates: n=60	during entire pregnancy or at least during the third trimester	Adjusted for sex, gestational age (±1 wk), birth weight, mode of delivery
Lewis 2010[39] Australia PC-Clinic Medium	Medication group N=27 Control group N=27 Types, doses, duration NR	NR	No adjustment for confounders
Logsdon, 2011[40] US, Pennsylvania PC Medium	Control (no SSRI, no MDD): N=144 Responder (SSRI, no MDD): N=48 Untreated (MDD, no SSRI): N=12 Nonresponder (Both MDD and SSRI): N=11	NR	Excluded from study: active substance abuse, benzodiazepines, prescription drugs in FDA-defined categories of D or X.
Louik 2007[41] US CC	Exposed: infants exposed to any SSRI (fluoxetine, sertraline, paroxetine, citalopram, non-SSRI antidepressant) n=9849 Control: infants without birth defects, n=5860 Dose and duration NR	First trimester-exposure to any SSRI from 28 days before the last menstrual period through the fourth lunar month (112 days after the last menstrual period)	Maternal age, maternal race or ethnic group (self reported), maternal education, year or last menstrual period, parity, study center, first-trimester smoking, first-trimester alcohol consumption, history of a birth defect in first degree relative, pre pregnant BMI, seizures, diabetes mellitus, hypertension, infertility, first trimester use of folic acid.
Lund, 2009[42] Denmark PC Medium	SSRI, N=329, duration and dose NR Control: Psychiatric history, no SSRI use: 4902 Control, No psychiatric history, no SSRI use: 51770	NR	Parity, maternal age, BMI, smoking habit, alcohol intake, marital status, education

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Malm, 2011[43] Finland TIS Low	SSRI (N=6,881, duration and dose NR) No SSRI (N=618,727, duration and dose NR)	1 month prior to pregnancy or during the first trimester	Adjusted for maternal age at end of pregnancy, parity, year of pregnancy ending, marital status, smoking during pregnancy, purchase of other reimbursed psychiatric drugs during the first trimester, maternal prepregnancy diabetes.
McFarland, 2011[44] US, Rhode Island PC Medium	Dose and duration NR MDD SRI (N=37) No SRI (N=28) Non-MDI SRI (N=15) No SRI (81)	During pregnancy	Excluded Axis I diagnosis Women with current anxiety disorder diagnosis or PTSD were included in MDD and non-MDD groups
Merlob, 2009[45] Israel TIS Medium	SSRI (N=235, duration and dose NR) No-SSRI (67,636, duration and dose NR)	First-trimester exposure	Excluded chromosomal defects
Misri 2006[46] Canada PC-Clinic Medium	SSRIs only (N=13) During Pregnancy: Fluoxetine 20.00 mg Paroxetine 23.57 mg Sertraline 91.67 mg Duration: 191 days During breastfeeding: Fluoxetine 26.67 mg Paroxetine 27.50 mg Sertraline 91.67 mg Duration: 59.46 days SSRIs plus clonazepam (N=9) During Pregnancy: Fluoxetine 15.00 mg Paroxetine 23.57 mg SSRI Duration: 167.78 days Clonazepam dose/duration: 0.67 mg/136.63 days During breastfeeding: Fluoxetine 26.56 mg Paroxetine 15.00 mg Sertraline 28.57 mg Duration: 60.13 days Clonazepam dose/duration: 0.71 mg/41.22 days	During pregnancy and breastfeeding	Depression, anxiety

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Misri 2010[47] Canada PC-Clinic Medium	Depressed and treated with antidepressants N=39 Individual drugs, % patients, mean dosages: Fluoxetine: 17%, 3.14 mg Paroxetine: 44%, 25.6 mg Sertraline: 15%, 91.7 mg Citalopram: 17%, 57.3 mg Venlafaxine: 7%, 87.5 mg days on SSRIs and/or SNRIs=222 Exposed to SSRIs and/or SNRIs at 3-month visit=26% and 6-month visit=11% Depressed and not treated with antidepressants, N=13 Not depressed and not treated with antidepressants	NR	NR
Mulder 2011[48] The Netherlands Prospective cohort/Data Source[PC] Medium	Exposed N=96, previously exposed N=37 44% paroxetine, 21% fluoxetine, 20% citalopram, 7% venlafaxine, 4% fluvoxamine, 4%sertraline median mDDD: 1 (range 0.2–3.0 mDDD) Duration: 6 months Control: Unexposed N = 130	Throughout pregnancy	Adjusted for fetal behavioral states and gestation.
Nakhai-Pour, 2010[49] Canada CC Low	Exposures: Selective Serotonin Reuptake Inhibitors (SSRI): citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline; Tricyclic Antidepressants: amitriptyline, desipramine, imipramine, nortriptyline; Serotonin-norepinephrine reuptake inhibitors: venlafaxine; Serotonin modulators; dopamine and norepinephrine reuptake inhibitors. Doses and Duration: NR Cases N= 5124 Controls N= 51240	Cases: First day of gestation through the calendar date of spontaneous abortion Controls: First day of gestation through the same gestation age as matched case	Adjusted for maternal age, social assistance status, place of residence, gestational age at index date, comorbidities (diabetes mellitus, CV disease, asthma, untreated thyroid disease, depression, anxiety and bipolar disorder), history of spontaneous abortion and therapeutic abortion, visits to psychiatrists, number of prescribers, number of visits to physicians, duration of exposure to antidepressants and other medications in the year before pregnancy, number of prenatal visits, visits to obstetricians and other medication use during pregnancy.
Nordeng, 2012[50] Norway PBR Medium	Exposed: N= 699 antidepressant use during pregnancy, 1,048 use prior to pregnancy only Unexposed: N=61,648	6 months before pregnancy; 1st trimester, 2nd and/or 3rd trimester, total pregnancy (includes use when timing during pregnancy unknown)	Level of maternal depression, maternal age at delivery, education, parity, prepregnancy BMI, maternal asthma or CV disease, NSAID use, folic acid use, and smoking during pregnancy.

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Nulman, 2002[83] Canada PC Medium	Exposed: N=46 tricyclic antidepressants, 40 fluoxetine Unexposed: N=36 nondepressed women	Throughout pregnancy	Mother's IQ, socioeconomic status, ethanol use and cigarette smoking, depression severity, depression duration, treatment duration, number of depressive episodes after delivery, and medications used for depression treatment.
Oberlander 2002[52] Canada Prospective cohort/Data Source [PC] Medium	Exposed group 1, N=22, and Group 2, N=16 Group 1: Paroxetine: 11 Fluoxetine: 7 Sertraline: 4 Group 2: Paroxetine + Clonazepam: 2 Fluoxetine + Clonazepam: 14 Dose: (median mg/day) Paroxetine: 20 (10-30) Fluoxetine: 20 (10-30) Sertraline: 62.5 (50-150) Group 2: Paroxetine + Clonazepam: 20 (10-30) + 05 (.25-1.175) Fluoxetine + Clonazepam: 20 (10-30) +.43 (.1-.75) Duration: NR Control: Unexposed N = 23	Pre and post partum	Not reported
Oberlander, 2006[53] Canada, British Columbia PBR Medium	Any SSRI (N=1451), fluoxetine 44.7%, sertraline 25.6%, fluvoxamine 4.6%, citalopram 3.3%. Depression, No SSRI (N=14234) No depression, No SSRI (N=92192)	SSRI prescription filled more than 49 days after conception	Propensity score matching used to draw a comparison sub-group from the depressed, no SSRI group that was similar in all measured maternal characteristics to the SSRI exposed group.
Oberlander, 2008[54] Canada, British Columbia PC Medium	SRI Exposure, N=37 Paroxetine, n=18 (Median dose, 27.5mg) Fluoxetine, n=6 (Median dose, 35mg) Sertraline, n=5 (Median dose, 100mg) Venlafaxine, n=3 (Median dose, 75mg) Citalopram, n=5 (Median dose, 30mg) Duration: 94.6% continued from prior to recruitment to delivery No Exposure, N=47	Throughout pregnancy	NR

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Oberlander, 2008[55] (Birth Defects Res Part B) Canada, British Columbia PBR Medium	Controls Depression alone: N=7,883 No exposure: N=10,702 Medication Groups SRI only Benzodiazepines only SRI + Benzodiazepines SRIs: Paroxetine, 37.0%; Sertraline, 24.3%; Fluoxetine, 24.2%; Venlafaxine, 7.1%; Fluvoxamine, 4.6%; Citalopram, 2.8%	First trimester: LMP to LMP plus 90 days	Controlled for maternal illness characteristics, diseases, and complications of pregnancy diagnosed more than 60 days before birth, depression in the first trimester, and a dummy variable indicating that the mother filled a prescription after she knew that she was pregnant, and a variable indicating whether the patient had been prescribed methadone, exposure to clonazepam or clobazam (sometimes used as anticonvulsants), exposure to antipsychotics, non-SRI antidepressants.
Okun, 2011[56] US, Ohio and Pennsylvania PC Medium	SSRI vs. No SSRI Total N: 240 20 weeks: 46 vs. 194 30 weeks: 46 vs. 159 36 weeks: 36 vs. 143 duration, doses NR	At 20, 30 and 36 weeks	NR
Okun, 2012[57] US, Ohio and Pennsylvania PC Medium	At enrollment (20 weeks) No MDD, No SSRI (N=135) No MDD, taking SSRI (N=26) MDD, No SSRI (N=35) MDD, taking SSRI (N=16) Dose, duration NR	at 20 and 30 weeks of pregnancy	Adjusted for the effect of depression and SSRI status at the time of assessment (week 20 or 30), as well as history of pre-term birth, age, marital status, and employment status.
Palmsten 2012[58] Canada RC-LD Medium	SSRI monotherapy, N=3,169 SSRI polytherapy, N=333 SNRI monotherapy, N=408 TCA monotherapy, N=146 No antidepressant therapy, N=65,392	During estimated gestational weeks 10 and 20	Adjusted for delivery year, age, diabetes, multifetal gestation, obesity, primiparity, and physician visits, number of depression claims, number of psychiatrist visits/mental health hospitalizations, and dispensing of benzodiazepines, anticonvulsants, and antipsychotics

Author, year Country Study Design/Data Source Risk of Bias	4. Exposures (N, duration, dose) Controls (N)	5. Exposure Period	6. Confounders
Pearson 2007[59] US, Louisiana Retrospective cohort Data/Source: [AD] Medium	Exposed: N=84 Total SSRI: N= 42 Escitalopram N= Fluoxetine N= 17 Sertraline N= 13 Paroxetine N= 12 Total Tricyclic Antidepressants: N= 37 Amitriptyline N= 2 Desipramine N= 7 Imipramine N= 11 Nortriptyline N= 13 Other: N= 5 Bupropion N= 2 Dose: NR Controls: Unexposed N=168	Conception only: 7.6% First and second trimesters: 15% Third trimester: 67% Throughout: 70%	Conception only: 7.6% First and second trimesters: 15% Third trimester: 67% Throughout: 70%
Pedersen, 2009[60] Denmark PBD, LD Medium	SSRI: fluoxetine n=348, citalopram n=460, Paroxetine n=299, Sertraline: n=259, more than 1 type of SSRI n=193, dose and duration NR Control: No unexposed infants n=493113	28 days before to 112 days after beginning of gestation	Adjusted for maternal age, calendar time, marital status, income and smoking.
Pedersen, 2010[61] Denmark PC Medium	Exposed N=415, SSRI only n=336, fluoxetine n=88, citalopram n=86, paroxetine n=76, sertraline n=86 Untreated N=489, depression with no psychotropic medication Unexposed N=81042, no exposure to psychotropic medication and no severe symptoms of depression	Entire pregnancy	Adjusted for maternal age, gender, age at interview, breastfeeding, problems during pregnancy, mother-child connection, postnatal symptoms of depression, and postnatal difficulties.
Rai 2013[62] Sweden CC Low	SSRIs=fluoxetine, citalopram, paroxetine, sertraline Non-selective monamine reuptake inhibitors (MRIs)=clomipramine, amitriptyline, nortriptyline Dose, duration NR Cases N=4,429 Controls N=43,277	During pregnancy	Adjusted for history of psychiatric disorders other than depression, parental ages, income, education, occupation, migration status, and parity.

Author, year Country Study Design/Data Source Risk of Bias	4. Exposures (N, duration, dose) Controls (N)	5. Exposure Period	6. Confounders
Ramos, 2008[84] Canada, Quebec LD Medium	Doses, durations NR Antidepressant use: First trimester, N=1101 Second trimester, N=510 Third trimester, N=476 Drugs: SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline); Tricyclics (amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, trimipramine); Other Antidepressants (bupropion, mirtazapine, moclobemide, nefazodone, trazodone, venlafaxine)	Throughout pregnancy	Adjusted for maternal age, being on welfare, urban dweller, living alone, measures related to psychiatric disorders and measures of comorbidities not related to psychiatric disorders before and during pregnancy, hypertension and diabetes diagnoses before and during pregnancy, gender of baby, prenatal visits and year of pregnancy.
Ramos, 2010[64] Canada, Quebec LD, supplemental questionnaire Medium	Doses, durations NR SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline); First trimester, N=851 Second trimester, N=458 Third trimester, N=434 Tricyclics (amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, trimipramine) First trimester, N=85 Second trimester, N=29 Third trimester, N=24 Other Antidepressants (bupropion, mirtazapine, moclobemide, nefazodone, trazodone, venlafaxine) First trimester, N=211 Second trimester, N=70 Third trimester, N=62 Co-exposure (2 classes or more) First trimester, N=109 Second trimester, N=33 Third trimester, N=30 No Antidepressants First trimester, N=1450 Second trimester, N=2116 Third trimester, N=2156	throughout pregnancy	Adjusted for: in the year prior to pregnancy: the number of different medications used other than ADs, the number of visits to the emergency department or hospitalizations, and the BMI; and on the first day of gestation and during pregnancy: maternal age, race, being a welfare recipient or not, area of residence, parity, income, marital status, maternal weight gain, tobacco, alcohol, and illicit drug use, and finally caffeine intake, pre-pregnancy and gestational diabetes, pre-pregnancy and gestational hypertension , and asthma. The following proxies were used: the number of days on antidepressants and the number of visits to the psychiatrist in the year prior to pregnancy; the number of different psychiatric disorder diagnoses received prior to and during pregnancy; the use of an anxiolytic or sedative such as benzodiazepines; and the use of an anticonvulsant such as carbamazepine during pregnancy. Stratified according to antidepressant dosage used during pregnancy.
Rampono, 2009[65] Australia PC Medium	Exposed: N=9 citalopram (median daily dose 20 mg), 8 escitalopram (20 mg), 6 sertraline (50 mg, fluoxetine (30 mg), 1 fluvoxamine (150 mg), 1 paroxetine (30 mg), 11 venlafaxine Controls: N=18	During pregnancy. Not specified.	None

Author, year Country Study Design/Data Source Risk of Bias	4. Exposures (N, duration, dose) Controls (N)	5. Exposure Period	6. Confounders
Reebye, 2002[66] Canada PC Medium	Exposure SSRI: N=24, duration: median 192 days, dose: 20mg/day SSRI+: N=14 days, duration median: 161 days, SSRI mean dose 19mg/day, Rivotril mean dose: 0.48mg/day Nonexposed, non depressed: N=24	During pregnancy	NR
Reis, 2010[67] Sweden PBR Medium	Exposed (early use): N=1664 tricyclics, 10,170 SSRIs, 37 MOAIs, 1,351 SNRIs, 10 unspecified antidepressants Exposed (later use): N=784 tricyclics, 4,809 SSRIs, 18 MOAIs, 538 SNRIs, 0 unspecified antidepressants	Early=before the first antenatal visit Later=during pregnancy	Year of delivery, maternal age, parity, smoking, BMI
Salisbury, 2011[68] US, Rhode Island PC Medium	Controls (N=56) MDD (N=20) MDD plus SRI (N=36): sertraline 52.8%, fluoxetine 25.0%, paroxetine 8.3%, venlafaxine 2.8%	SRI use for at least 4 consecutive weeks during the second and/or third trimesters	Adjusted for gestational age at birth, age at NNNS assessment.
Salkeld 2008[69] Canada CC-LD Low	SSRI or non-SSRI: dose and duration NR Cases N=2460 Controls N=23,943	Third trimester: Prescription within 90 days of delivery	Adjusted for previous postpartum hemorrhage, multiple pregnancy, prolonged labor, abnormalities of the forces of labor, obstructed labor, perineal laceration or other gynecologic laceration, other obstetric trauma, placenta previa, placental abruption, and hypertensive disorders of pregnancy
Simon 2002[70] U.S. RC-HCDB Low	Tricyclic antidepressants (N=209): Amitriptyline N=66, imipramine N=49, doxepin N=36, nortriptyline N=33, desipramine N=22 SSRIs (N=185): Fluoxetine N=129, sertraline N=32, paroxetine N=28 Dose, duration NR	Any antidepressant prescription during the 270 days before delivery	Matched based on maternal age, year of delivery, lifetime use of antidepressants, and lifetime history of psychiatric treatment. Adjustment for maternal tobacco use, other substance use, race, and number of prior births.
Sit, 2011[71] US, Pennsylvania PC Medium	SRI (N=21) Sertraline, n=9 Venlafaxine, n=2 Escitalopram, n=2 Citalopram, n=1 Nortriptyline, n=1 Fluvoxamine, n=1 Fluoxetine, n=5 Doses, durations NR	Throughout pregnancy	Smoking
Stephansson, 2013[72] Sweden PBR Medium	Exposed: N=29,228 Controls: N=1,604,649	T0 (from 3 months before until last menstrual period before pregnancy), 1st trimester, 2nd trimester, 3 trimester	Smoking, country and year of birth, maternal age, birth order, maternal diabetes and hypertension, previous psychiatric hospitalization

Author, year Country Study Design/Data Source Risk of Bias	4. Exposures (N, duration, dose) Controls (N)	5. Exposure Period	6. Confounders
Suri, 2007[73] US, California PC Medium	Durations, NR Dose Groups: High (≥ 300mg bupropion; ≥ 225mg venlafaxine; ≥ 150mg sertraline; ≥ 100mg nortriptyline; ≥ 40mg citalopram, fluoxetine, paroxetine; ≥ 20mg escitalopram) Low-Medium: Any doses lower than in high group. MDD, antidepressant >50% of pregnancy (N=49) Monotherapies: Sertraline, n=15; Fluoxetine, n=13; Citalopram, n=4;Paroxetine, n=4; Venlafaxine, n=2; Nortriptyline, n=1 Sequential therapy: Citalopram/fluoxetine, n=1; Paroxetine/sertraline, n=1; Escitalopram/citalopram, n=1; Nefazodone/fluoxetine, n=1; Venlafaxine/sertraline, n=1; Fluoxetine/citalopram/sertraline, n=1; Citalopram/fluoxetine/sertraline, n=1; Venlafaxine/fluoxetine/sertraline, n=1 Concurrent therapy: Sertraline/venlafaxine, bupropion, n=1 Venlafaxine/nefazodone, then sertraline, n=1 MDD, no antidepressant or discontinued during first trimester and/or <10 days exposure (N=22) First trimester only: Sertraline, n=3; Venlafaxine, n=2; Fluoxetine, n=1 6 weeks of first trimester + 9 days second trimester, Citalopram, n=1 Second trimester, seven days, sertraline, n=1 No psychiatric history, controls (N=19)	Entire pregnancy	Controlled for maternal age, number of previous pregnancies, historical and developing risk factors for preterm birth, hypertension, pregnancy-induced hypertension, pre-eclampsia and maternal weight gain.
Suri, 2011[74] US, California PC Medium	MDD, with antidepressant (N=33) Fluoxetine: 38%, Daily dose M=22.5mg/day Sertraline: 36%, Daily dose M=90.5mg/day MDD, no antidepressant (N=16) No MDD, no antidepressant (N=15)	throughout pregnancy	Adjusted for GA at delivery
Toh, 2009[75] US CC Medium	Exposed: N=92 who continued SSRI exposure, 107 who discontinued SSRI exposure Controls: N=5,532 with no SSRI exposure	Discontinued exposure=Treated 2 months before pregnancy but discontinued before the end of the 1st trimester Continued exposure=Treated 2 months before pregnancy and continued after the 1st trimester	Region, birth year, maternal age, race/ethnicity, education, family income, gravidity, number of fetuses, prepregnancy BMI, age at menarche, diabetes mellitus, infertility treatment, cigarette smoking, coffee and alcohol intake, use of illicit drugs or other psychotherapeutic medications during pregnancy.

Author, year Country Study Design/Data Source Risk of Bias	4. Exposures (N, duration, dose) Controls (N)	5. Exposure Period	6. Confounders
Ververs, 2009[76] the Netherlands AD Medium	Any antidepressant (N=784) SSRI total, n=557 Paroxetine, n=305 Fluoxetine, n=110 Tricyclic antidepressant, n=109 Other antidepressant, n=118 Dose, Duration, NR	Continuous Users: Used antidepressant before and throughout pregnancy Starters: No antidepressant use in the 6 months prior to pregnancy, but used them during pregnancy Stoppers: Antidepressant used before pregnancy, but did not do so during pregnancy Irregular Users: Any other pattern of antidepressant use during pregnancy Non-Users: No antidepressant use before or during pregnancy	NR
Wen 2006[77] Canada RC, PBD Medium	SSRI: citalopram n=14, Fluoxetine: n=973, Fluvoxamine:204, Paroxetine: 563, Sertraline: 395 Duration and dose NR	1 year before delivery	Year of birth, type of institute at birth, (base, community, tertiary center), first 3 digits of mother's postal code
Wilson, 2011[78] US CC Medium	Cases: N=20 Controls: N=120	After 20 weeks gestation	Maternal age, parity, neonatal gender, tobacco use, mode of delivery, diabetes (preexisting and gestational), chorioamnionitis, obesity
Wisner, 2009[79] US, Ohio Prospective cohort Medium	Any SSRI No SSRI, no depression (N=131) 2. Continuous SSRI exposure (N=48) 3. Continuous depression, no SSRI (N=14) 4. Partial SSRI exposure (N=23) 5. Partial depression, no SSRI (N=22)	Groups formed by the following definitions: No SSRI, no depression: no exposure to any antidepressant or to major depressive disorder. 2. Continuous SSRI exposure: treatment with an SSRI during the entirety of pregnancy or for the majority of each of the three trimesters. 3. Continuous depression, no SSRI: the presence of major depression throughout pregnancy or for the majority of each of the three trimesters, without SSRI treatment. 4. Partial SSRI exposure: treatment with an SSRI at some point during pregnancy but at least one full trimester without exposure; this group was equally split between women treated with an SSRI in the first and/or second trimester, but not the third, and women treated in the second and/or third trimester, but not the first. 5. Partial depression, no SSRI: major depressive disorder at some point during pregnancy but no depression for at least one trimester, without SSRI treatment	maternal age and race, Prepregnancy BMI, weight gain at week 36, and infant birth weight, preterm birth, NICU admission, 1- and 5-minute Apgar scores of 7 or less, Peripartum Events Scale subscale ratings of 2 or higher, and respiratory signs

Author, year **Country** **Study Design/Data Source** **Risk of Bias**	**4. Exposures (N, duration, dose)** **Controls (N)**	**5. Exposure Period**	**6. Confounders**
Wogelius, 2006[80] Denmark PBR Medium	Exposed: N=1051 within 1st trimester or 30 days before, 453 within 2nd or 3rd month after conception Controls: N=150,780	Within 1st trimester or 30 days before, within 2nd or 3rd month after conception	Maternal smoking during pregnancy, birth order, maternal age, prescriptions for antiepileptics, antidiabetics and NSAIDS during pregnancy, birth year, country, length of gestation
Yonkers 2012[81] US Prospective Cohort [PC] Low	Exposed: N= 320 SSRI: Citalopram N=26 Escitalopram N=47 Fluoxetine N=68 Sertraline N=121 Paroxetine N=21 Other: Venlafaxine N=29 Duloxetine N=8 Dose: NR	First trimester only Second trimester and third trimester only Throughout	Adjusted for mother's age, education, race, smoking, illicit drug use, history of preterm birth. Second adjusted analysis additionally included psychiatric illness history, severity of disease, concurrent diagnoses.
Zeskind 2004[85] US Prospective cohort study/Data Source [PC, AD] Medium	N=17 Celexa N= 5, Prozac N= 1, Paxil N= 3, Zoloft N= 5; sequential combination of Paxil, Prozac, and Zoloft N= 1 or Paxil N= 1; or Paxil and Zoloft N= 1 in combination with Wellbutrin. Duration NR Control: Unexposed N = 17	Throughout pregnancy	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Alwan 2007[1] US Arm of Case Control Studied, Population based Medium	No increase in congenital heart defects with SSRI. + association anencephaly, craniosynostosis, omphalocele	NR	NR
Alwan 2010[2] Canada Case-control/Data Source[CC] Medium	Maternal Bupropion use among infants with categories of heart defects: Adjusted OR (95% CI) Conotruncal heart defects: 0.9 (0.3–2.6) Tetralogy of Fallot: 1.5 (0.4–5.1) Left outflow tract heart defects: 2.6 (1.2–5.7) Coarctation of aorta: 2.6 (1.0–6.9) Hypoplastic left heart: 2.7 (0.8–9.1) Right outflow tract heart defects: 1.2 (0.4–3.4) Pulmonary valve stenosis: 1.1 (0.3–3.8) Septal heart defects: 1.4 (0.7–2.8) Perimembranous VSD: 1.2 (0.5–3.4) ASD secundum: 1.1 (0.4–3.0) ASD nos: 2.2 (0.6–7.5) All groups of heart defects in NBDPS: 1.4 (0.8–2.5)	NR	NR
Andrade, 2009[86] US Retrospective Cohort/Data Source [AD] Medium	Persistent pulmonary hypertension, (unadjusted) Prevalence ratio (95% CI) SSRI: PPHN among exposed was 2.14 per 1000 (95% confidence interval (CI) 0.26, 7.74) vs. not exposed was 2.72 per 1000 (95%CI 0.56, 7.93)	NR	NR
Bakker 2010[4] CC/PBD Netherlands Medium	Congenital defects, comparison to not exposed: All heart defects: OR, 1.5; P=0.476; 95% CI, 0.5 to 4.0 VSD: AOR, 0.5; P=0.528; 95% CI, 0.1-4.2 ASD: AOR, 5.7: P=0.016; 95% CI, 1.4-23.7 Septal defects (includes ASD and VSD): AOR, 1.6; P=0.493; 95% CI, 0.4-5.6 Right-sided defects: AOR, 0.9; P=0.926; 95% CI, 0.1-7.6 Left-sided defects: AOR, 2.1; P=0.292; 95% CI, 0.5-8.7 Other defects: AOR, 1.0; P=0.967; 95% CI, 0.2-5.2	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Bakker 2010[5] The Netherlands Case-Control Medium	Adjusted ORs (95% CI) for cases and controls: All heart defects: 1.5 (0.5-4.0) VSD: 0.5 (0.1-4.2) ASD: 5.7 (1.4-23.7) Septal defects: 1.6 (0.4-5.6) Right-sided defects: 0.9 (0.1-7.6) Left-sided defects: 2.1 (0.5-8.7) Other defects: 1.0 (0.2-5.2)	NR	NR
Ban, 2012[6] U.K. PBD Medium	Adjusted RRR (99% CI) Referent category: No history of or current depression or anxiety A. Unmedicated mental illness B. TCA C. SSRI Perinatal death: A: 1.4 (0.8 to 2.5), B: 1.6 (0.9 to 2.9), C:1.6 (1.1 to 2.4) Miscarriage: A: 1.0 (0.9 to 1.2), B: 1.3 (1.1 to 1.5), C:1.5 (1.3 to 1.6) Termination: A: 1.0 (0.9 to 1.2), B: 1.7 (1.5 to 1.9), C: 2.2 (2.1 to 2.4) Referent category: Unmedicated depression or anxiety during 1st trimester of pregnancy Perinatal death: B: 1.2 (0.5 to 2.7), C. 1.2 (0.6 to 2.3) Miscarriage: B. 1.3 (1.1 to 1.5), C: 1.4 (1.2 to 1.7) Termination:B.1.4 (1.2 to 1.7), C: 2.0 (1.8 to 2.3)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Berard, 2007[7] Canada, Quebec LD Medium	Adjusted ORs for Major Congenital malformations: Paroxetine vs. Other antidepressants: OR, 1.32; 95%CI, 0.79 to 2.20 Other SSRI vs. Other antidepressants: OR, 0.93; 95% CI, 0.53 to 1.62 2nd trimester exposure to any antidepressants vs. no 2nd trimester exposure: OR, 1.23; 95%CI, 0.62 to 2.43 3rd trimester exposure to any antidepressants vs. no 3rd trimester exposure: OR, 0.53; 95%CI, 0.25 to 1.11 Adjusted ORs for Major Cardiac Malformations: Paroxetine vs. Other antidepressants: OR, 1.38; 95%CI, 0.49 to 3.92 Other SSRI vs. Other antidepressants: OR, 0.89; 95%CI, 0.28 to 2.84 2nd trimester exposure to any antidepressants vs. no 2nd trimester exposure: OR, 0.72; 95%CI, 0.17 to 3.01 3rd trimester exposure to any antidepressants vs. no 3rd trimester exposure: OR, 0.46; 95%CI, 0.09 to 2.30 Adjusted ORs by Dose of Paroxetine (mg/day vs. no use) Major Congenital Malformations >0 to 20: OR, 0.71; 95%CI, 0.29 to 1.71 >20-25: OR, 1.30; 95%CI, 0.76 to 2.25 >25: OR, 2.23; 95%CI, 1.19 to 4.17 Major Cardiac Malformations >0 to 20: OR, 1.76; 95%CI, 0.45 to 6.82 >20-25: OR, 0.61; 95%CI, 0.13 to 2.88 >25: OR, 3.07; 95%CI, 1.00 to 9.42	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Bogen 2010/companion Wen 2009[8] U.S. PC	NR	NR	SRI at enrolment and infant feeding intention (N=168) RRR, 95%CI Breast and formula: 2.55 (0.85 to 7.66) Formula only: 12.31 (2.50 to 60.66), p=0.002 Unsure: 4.72 (1.01 to 21.9) Association between breastfeeding initiation and SRI use at enrolment and delivery: p>0.22 Association between breastfeeding at 2 weeks and not taking SRI at 2 weeks postpartum: p=0.04 SRI use at 2 weeks postpartum and its correlation to breastfeeding status at 12 weeks postpartum (n=99) HDRS<9: stopped breast feeding 12.0 (1.64 to 88.3) HDRS>9: Stopped breast feeding 0.28 (0.04 to 1.71)
Boucher, 2008[9] Canada LD Medium	Adjusted OR (95% CI) Symptoms in neonates exposed vs not exposed to antidepressants in late pregnancy: Alertness: 37 (8-174) Muscular tone: 20 (5-71) Neurological function: OR not computed because of 0 value in unexposed group, P<0.006 (unadjusted) Feeding, GI: 3.8 (1.7-8.1) Respiratory function: 2.5 (1.1-5.3) Serotonergic/adrenergic activity: 4.1 (1.1-15.5) Global (one or more of the above symptoms): 7.0 (3.2-15.3)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Casper 2003[10] US, California Cohort study Data/Source: [CC] Medium	Mean birth weight: Not exposed= 3363 (498.5) vs. exposed= 3394 (432.2) P=0.84 Birth length (cm): 49.7 (7.2) vs. 50.3 (2.5) P= 0.78 Gestational age (wk): 38.7 (1.5) vs. 39.1 (1.1) P= 0.38 Weight (%) 46.7 (27.4) vs. 48.4 (29.4) P=0.86 Height (%) 49.7 (30.1) vs. 41.9 (28.0) P= 0.42 Fronto-occipital circumference % 50.3 (28.1) vs. 54.2 (25.9) P= 0.66 Bayley scales: mean (SD) MDI 94.3 (7.5) vs. 91.0 (13.3) P= 0.27 PDI 98.2 (9.1) vs. 90.0 (11.4) P= 0.76 BRS 89.5 (15.4) vs. 76.0 (24.6) P=0.72 Major structural anomalies: 1 bilateral lacrimal duct stenosis (unexposed infant) 1 small asymptomatic ventricular septal defect (exposed infant) Minor structural anomalies: 54% unexposed and 76% of exposed infants ($\chi 2 = 0.18$; P =.17). 3 or more minor structural anomalies: 15% of unexposed 29% of exposed infants ($\chi 2 = 0.19$; P = .37).	Gross motor movement: mean (SD) 4.77 (.44) 4.43 (.68) P= 0.17 Fine motor movement: mean (SD) 5.00 (0) 4.71 (.46) P= 0.15 Control of movement: mean (SD) 4.77 (.44) 4.60 (.56) P = 0.46 Tremulousness: mean (SD) 5.00 (0) 4.87 (.34) P= 0.08 Slow and delayed movement: mean (SD) 4.92 (.28) P= 0.06 Frenetic movement: mean (SD) 5.00 (0) 4.87 (.43) P= 0.15 Hypertonicity: mean (SD) 5.00 (0) 4.97 (.18) P= 0.40 Hypotonicity: mean (SD) 4.92 (.28) 4.90 (.31) P= 0.83	Delivery and postpartum parameters: Breastfeeding average duration 6.4 ± 5.9 months (unexp) vs. 8.5 ± 7.2 (exp) t = 0.85; P = 0.4

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Chambers, 1996[11] US, California CC Medium	Infants Exposed in First Trimester vs. Control Infants: Major malformations (ventricular septal defect, ventricular septal defect with bilateral cryptorchidism, atrial septal defect, nasal dermoid sinus, coccygeal dermal sinus, hypospadias, bilateral inguinal hernia, cleft palate): 3.7% vs. 2.7%, p=0.57 Deformations (sagittal synostosis, bilateral hip dysplasia, unilateral hip dysplasia): 1.8% vs. 0.9%, p=0.65 All major structural anomalies combined: 5.5% vs. 4.0%, p=0.63 Infants Exposed in Exposed Early group vs. Exposed Late group vs. Control group Pre-term birth (<37 weeks): 4.1% vs. 14.3% vs. 5.9%, p=0.03 Admission to special care nursery: 11.9% vs. 31.5% vs. 8.8%, p<0.001 Birth weight, g: 3589 vs. 3392 vs. 3556, p=0.04 Birth weight <10th percentile: 3.2% vs. 11.5% vs. 3.3%, p=0.02 Birth length, cm: 51.5 vs. 50.4 vs. 51.5, p=0.01 Head circumference, cm: 34.8 vs. 34.3 vs. 34.5, p=0.19 Microcephaly, <3rd percentile: 2.2% vs. 3.3% vs. 1.0%, p=0.41 Adjusted RRs for Infants Exposed Late vs. Infants Exposed Early Prematurity: RR, 4.8; 95% CI, 1.1 to 20.8 Admission to special care nursery: RR, 2.6; 95% CI, 1.1 to 6.9 Poor neonatal adaption: RR, 8.7; 95% CI, 2.9 to 26.6	NR	NR
Chambers, 2006[12] US CC Medium	Definite PPHN, adjusted OR (95% CI): <u>Maternal use of antidepressants</u> Never used during pregnancy: 1.0 Any time during pregnancy: 1.4 (0.8, 2.5); P=0.30 SSRI: 1.6 (0.8, 3.2); P=0.16 Other antidepressants:1.8 (0.2, 2.7); P=0.76 <u>Maternal use of antidepressants</u> Never during pregnancy: 1.0 Before week 20: 0.6 (0.2, 1.5); P=0.28 After week 20: 3.2 (1.3, 7.4); P=0.008 <u>Maternal use of SSRIs</u> Never during pregnancy: 1.0 Before week 20: 0.3 (0.1, 1.2); P=0.08 After week 20: 6.1 (2.2, 16.8); P=0.001	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Cole 2007[13] US Case-control/Data Source[AD] Low	All congenital malformations: Monotherapy paroxetine group compared with other: Adjusted odd ratio: 1.89 (95%CI 1.20–2.98) Mono- or polytherapy paroxetine group compared with other: Adjusted odd ratio: 1.76 (95%CI 1.18–2.64) Cardiovascular malformations: Monotherapy paroxetine group compared with other Adjusted odd ratio: 1.46, 95%CI 0.74–2.88 Mono or polytherapy paroxetine group compared with other Adjusted odd ratio: 1.68, 95%CI 0.95–2.97 Prevalence of all congenital malformations: Monotherapy paroxetine group compared with other: Adjusted odd ratio:1.89, 95%CI 1.20–2.98 Mono- or polytherapy paroxetine group compared with other: 1.76, 95%CI 1.18–2.64 Subset of infants without maternal drugs known or suspected to be teratogenic: Monotherapy paroxetine group compared with other Adjusted odd ratio: 2.03, 95%CI 1.26–3.25 Mono or polytherapy paroxetine group compared with other Adjusted odd ratio: 1.79, 95%CI 1.17–2.73	NR	NR
Cole, 2007[14] US LD Medium	Congenital malformations, adjusted OR (95% CI) All congenital malformations Bupropion, 1st trimester: -- Other antidepressant, 1st trimester: 0.95 (0.62, 1.45) Bupropion, outside 1st trimester: 1.00 (0.57, 1.73) CV malformations Bupropion, 1st trimester: -- Other antidepressant, 1st trimester: 0.97 (0.52, 1.80) Bupropion, outside 1st trimester: 1.07 (0.48, 2.40)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Colvin 2012[15] PBD/CC Australia Medium	APGAR at 5 minutes Preterm birth (<37 weeks), adjusted OR (95% CI), comparison to not exposed: T1: AOR, 1.10; 95% CI, 0.88 to1.37 T2 or T3: AOR, 1.28; 95% CI, 0.97 to 1.70 Any: AOR, 1.48 ; 95% CI, 1.28 to 1.72 Birthweight (<2500g) adjusted OR (95% CI), comparison to not exposed: T1: AOR, 1.10; 95% CI, 0.88 to 3.8 T2 or T3: AOR, 1.46; 95% CI, 1.06 to 2.02 Any: AOR, 1.19; 95% CI 0.99 to1.43 Birth length (<=1798), OR (95% CI), comparison to not exposed: T1: OR, 1.52; 95% CI, 1.40 to1.65 T2 or T3: OR, 1.53; 95% CI, 1.34 to 1.74 Any: OR, 1.52; 95% CI, 1.42 to 1.63 Mean gestation, wks, t-test, comparison to not exposed: T1: <0.0001 T2 or T3: <0.0001 Any: <0.0001 Mean birth weight, g, t-test, comparison to not exposed: T1: <0.0001 T2 or T3: <0.0001 Any: <0.0001 Mean birth length, cm, t-test, comparison to not exposed: T1: <0.0001 T2 or T3: <0.0001 Any: <0.0001	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Colvin 2012[15] Australia ……(Cont)	Death before one year, comparison to not exposed: overall: OR, 1.38; 95% CI, 1.06 to 1.81 citalopram: OR, 1.08; 95% CI, 0.64 to 1.84 paroxetine: OR, 1.44; 95% CI, 0.79 to 2.63 sertraline: OR, 1.45; 95% CI, 0.95 to 2.22 fluoxetine: OR, 1.45; 95% CI, 0.65 to 3.26 escitalopram: OR, 1.85; 95% CI, 0.76 to 4.49 fluvoxamine: OR, 1.89; 95% CI, 0.60 to 5.95 Stillbirths, comparison to not exposed: overall: OR, 1.07; 95% CI, 0.72 to 1.58 citalopram: OR, 0.93; 95% CI, 0.44 to 1.97 paroxetine: OR, 0.90; 95% CI, 0.34 to 2.42 sertraline: OR, 1.48; 95% CI, 0.85 to 2.57 fluoxetine: OR, 0.83; 95% CI, 0.21 to 3.35 escitalopram: OR, 0.63; 95% CI, 0.09 to 4.51 fluvoxamine: 0 Any major birth defect: OR, 0.52; 95% CI, 0.21 to 1.28		
Croen, 2011[16] US, California CC Medium	NR	Adjusted OR for Risk of Autism Spectrum Disorder vs. Unexposed in year before delivery Any antidepressant: OR, 2.0; 95%CI, 1.2 to 3.6 Any SSRI: OR, 2.2; 95%CI, 1.2 to 4.3 SSRI only: OR, 2.6; 95%CI, 1.3 to 5.4 Tricyclics and/or Dual-Action: OR, 1.6; 95%CI, 0.5 to 4.5 Adjusted OR for Risk of Autism Spectrum Disorder for SSRI use by trimester vs. Unexposed in year before delivery Preconception period: OR, 2.1; 95%CI, 1.1 to 4.2 First trimester: OR, 3.8; 95%CI, 1.8 to 7.8 Second trimester: OR, 1.9; 95%CI, 0.7 to 5.6 Third trimester: OR, 2.9; 95%CI, 1.0 to 8.0 year before delivery: OR, 2.2; 95%CI, 1.2 to 4.2	NR
Davidson, 2009[17] Israel CC Medium	SSRI vs. Controls GA: 38.6 vs. 38.9, NSD Birth weight, g: 3173 vs. 3333, NSD Birth length, cm: 49.0 vs. 50.4, p=0.008 Head circumference, cm: 33.8 vs. 34.4, p=0.08 Birth weight <10th percentile: 29% vs. 5%, p=0.045 Birth length <10th percentile: 14% vs. 0%, p=0.08 Head circumference <10th percentile: 19% vs. 0%, p<0.04 Discharge day: 3.9 vs. 2.7, p=0.005	NR	SSRI vs. Controls Weight gain (kg): 62.7 vs. 64.5, NSD

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Davis, 2007[18] US LD Medium	At 30 days: RRs, SSRI vs. No SSRI Preterm delivery: RR, 1.45; 95%CI, 1.25 to 1.68 One or more perinatal event of interest: RR, 1.16; 95%CI, 1.06 to 1.26 Fetal distress: RR, 6.00; 95%CI, 1.88 to 19.18 Excessive fetal growth: RR, 6.27; 95%CI, 0.83 to 47.43 Polyhydramnios: RR, 29.35; 95%CI, 3.30 to 261.08 Polyhydramnios and oligohydramnios: RR, 8.34; 95%CI, 1.94 to 35.80 Complications of placenta, cord, and membranes: RR, 0.69; 95%CI, 0.31 to 1.54 Complications of delivery, including malpresentation and malformation: RR, 1.42; 95%CI, 1.05 to 1.93 Disorders related to gestational age and birth weight: RR, 0.92; 95%CI, 0.68 to 1.26 Birth trauma: RR, 1.51; 95%CI, 1.04 to 2.20 Intrauterine hypoxia and asphyxia: RR, 1.38; 95%CI, 0.93 to 2.06 Respiratory distress syndrome and other respiratory conditions: RR, 1.97; 95%CI, 1.65 to 2.35 Neonatal hemorrhage and hemolytic diseases of the newborn: RR, 1.09; 95%CI, 0.69 to 1.70 Other causes of perinatal jaundice: RR, 0.91; 95%CI, 0.76 to 1.09 Endocrine and metabolic disturbances specific to newborn, including neonatal hypoglycemia: RR, 1.61; 95%CI, 1.15 to 2.27 Disorders of the digestive system: RR, 0.52; 95%CI, 0.07 to 3.68 Disorders of temperature regulation, including hypothermia: RR, 1.56; 95%CI, 1.06 to 2.31 Convulsions in the newborn: RR, 2.60; 95%CI, 1.16 to 5.84 Feeding problems in the newborn: RR, 1.26; 95%CI, 0.97 to 1.65 Other conditions: RR, 1.41; 95%CI, 1.12 to 1.78 Observation and evaluation of newborns for suspected condition not found: RR, 2.22; 95%CI, 1.70 to 2.90 One or more perinatal event of interest: RR, 1.16; 95%CI, 1.06 to 1.26	At 365 days: RRs, SSRI vs. No SSRI One or more malformation of interest: RR, 0.97; 95%CI, 0.81 to 1.16 Spina Bifida: RR, 2.21; 95%CI, 0.30 to 16.00 Other congenital anomalies of nervous system: RR, 1.98; 95% CI, 0.94 to 4.19) Congenital anomalies of the eye: RR, 1.33; 95%CI, 0.82 to 2.17 Congenital anomalies of ear, face and neck: RR, 0.37; 95%CI, 0.27 to 2.60 Bulbus cordis anomalies and anomalies of cardiac septal closure: RR, 0.93; 95%CI, 0.50 to 1.73 Other congenital anomalies of the heart: RR, 0.88; 95%CI, 0.42 to 1.86) Other congenital anomalies of circulatory system: RR, 1.55; 95%CI, 0.83 to 2.90 Congenital anomalies of respiratory system: RR, 0.23; 95%CI, 0.03 to1.68 Cleft palate and cleft lip: RR, 2.22; 95%CI, 0.69 to 7.08 Other congenital anomalies of upper alimentary tract: RR, 1.25; 95%CI, 0.65 to 2.42 Other congenital anomalies of digestive system: RR, 1.37; 95%CI, 0.44 to 4.27 Congenital anomalies of genital organs: RR, 0.82; 95%CI, 0.50 to 1.34 Congenital anomalies of urinary system: RR, 0.93; 95%CI, 0.44 to 1.96 Certain congenital musculoskeletal deformities: RR, 0.76; 95%CI, 0.46 to 1.26 Other congenital anomalies of limbs: RR, 0.67; 95%CI, 0.35 to 1.29 Other congenital musculoskeletal anomalies: RR, 0.60; 95%CI, 0.29 to 1.27 Congenital anomalies of the integument: RR, 0.89; 95%CI, 0.46 to 1.71 Other and unspecified congenital anomalies: RR, 0.84; 95%CI, 0.32 to 2.24	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Davis, 2007[18] ……..(Cont)	CONTINUED..... RRs, Tricyclics vs. No tricyclics Preterm delivery: RR, 1.67; 95%CI, 1.25 to 2.22 One or more perinatal event of interest: RR, 1.25; 95%CI, 1.03 to 1.51 Complications of placenta, cord, and membranes: RR, 1.44; 95%CI, 0.36 to 5.72 Complications of delivery, including malpresentation and malformation: RR, 1.46; 95%CI, 0.70 to 3.02 Disorders related to gestational age and birth weight: RR, 1.29; 95%CI, 0.67 to 2.51 Birth trauma: RR, 1.81; 95%CI, 0.76 to 4.30 Intrauterine hypoxia and asphyxia: RR, 1.03; 95%CI, 0.34 to 3.13 Respiratory distress syndrome and other respiratory conditions: RR, 2.02; 95%CI, 1.33 to 3.06 Neonatal hemorrhage and hemolytic diseases of the newborn: RR, 2.12; 95%CI, 0.97 to 4.64 Other causes of perinatal jaundice: RR, 1.02; 95%CI, 0.67 to 1.54 Endocrine and metabolic disturbances specific to newborn, including neonatal hypoglycemia: RR, 2.15; 95%CI, 1.04 to 4.44 Disorders of the digestive system: RR, 3.08; 95%CI, 0.43 to 21.89 Disorders of temperature regulation, including hypothermia: RR, 2.36; 95%CI, 1.08 to 5.16 Convulsions in the newborn: RR, 2.76; 95%CI, 0.39 to 19.54 Feeding problems in the newborn: RR, 1.69; 95%CI, 0.96 to 2.97 Other conditions: RR, 1.71; 95%CI, 1.02 to 2.86 Observation and evaluation of newborns for suspected condition not found: RR, 1.07; 95%CI, 0.41 to 2.81 One or more perinatal event of interest: RR, 1.25; 95%CI, 1.03 to 1.51	CONTINUED..... RRs, Tricyclics vs. No tricyclics One or more malformation of interest: RR, 0.86; 95%CI, 0.57 to 1.30 Spina bifida: RR, 12.43; 95%CI, 1.70 to 90.66 Other congenital anomalies of nervous system: RR, 1.27; 95%CI, 0.18 to 8.99 Bulbus cordis anomalies and anomalies of cardiac septal closure: RR, 0.92; 95%CI, 0.23 to 3.70 Other congenital anomalies of circulatory system: RR, 0.74; 95%CI, 0.10 to 5.29 Congenital anomalies of respiratory system: RR, 1.09; 95%CI, 0.15 to 7.72 Other congenital anomalies of upper alimentary tract: RR, 1.29; 95%CI, 0.32 to 5.15 Other congenital anomalies of digestive system: RR, 2.49; 95%CI, 0.35 to 17.50 Congenital anomalies of genital organs: RR, 0.77; 95%CI, 0.25 to 2.38 Congenital anomalies of urinary system: RR, 0.64; 95%CI, 0.09 to 4.53 Certain congenital musculoskeletal deformities: RR, 1.42; 95%CI, 0.65 to 3.12 Other congenital anomalies of limbs: RR, 2.55; 95%CI, 1.23 to 5.29 Other congenital musculoskeletal anomalies: RR, 0.82; 95%CI, 0.21 to 3.24 Other and unspecified congenital anomalies: RR, 0.92; 95%CI, 0.13 to 6.49	

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Dubnov-Raz, 2008[19] Israel CC Medium	SSRI vs. Control GA: 39 vs. 39, p=0.84 Birth weight, g: 3135 vs. 3365, p=0.04 ECG results, SSRI vs. Control Heart rate, bpm: 129 vs. 138, p=0.01 PR interval, ms: 98 vs. 100, p=0.31 QRS duration, ms: 51 vs. 52, p=0.28 QT interval, ms: 280 vs. 261, p<0.001 QTc interval, ms: 409 vs. 392, p=0.02 JT interval, ms: 229 vs. 209, p<0.001 Pathologically prolonged QTc interval (462-543ms): 10% vs. 0.0%, p=0.057	NR	NR
Dubnov-Raz, 2012[20] Israel CC Medium	Adjusted Difference scores for infant birth outcomes, SSRI vs. Control: Birth weight, g: -96; 95% CI, -257 to 65; p=0.20 Birth weight, z-score: -0.31; 95% CI, -0.71 to 0.10; p=0.14 Length: -0.74; 95%CI, -1.53 to 0.06; p=0.07 Head circumference: -0.72; 95%CI, -1.22 to 0.22 Adjusted Difference scores for infant tibial bone density, SSRI vs. Control: Speed of sound (m/s): 3.8; 95%CI, -52 to 60 Speed of sound (z-score): 0.01; 95%CI, -0.47 to 0.50	NR	NR
El Marroun 2012[21] Netherlands Prospective Cohort*Data Source [PC and PD] Low	Exposed higher risk for preterm birth (OR=2.14; 95% CI: 1.08 to 4.25; P=.03) Fetal Weight Gain: (Adjusted decrease weight, g 95% CI) Exposed:−2.3 (−7.0 to 2.3) P=0.32 Unexposed: −4.4g (−6.3 to −2.4) p<.001 Fetal Head Growth: (Adjusted decrease circumference, mm, 95% CI) Exposed: −0.18 (−0.32 to −0.07) P= 0.003 Unexposed: −0.08 (−0.14 to −0.03) P= 0.003 Head Circumference at Birth: Exposed: −5.88 (−11.45 to −0.30) P= 0.04 Unexposed: 0.05 (−3.48 to 4.43) P= 0.81 Control group (reference)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Ferreira 2007[22] US Retrospective Cohort/Data Source[AD] Medium	Neonatal behavioral signs (Adjusted OR, 95% CI): 3.1 (1.3–7.1) Prematurity (Adjusted OR, 95% CI): 3.9 (1.6–9.5) 2.4 (0.9–6.3) Admission to specialized care (Adjusted OR, 95% CI): 2.4 (0.8–6.9) Malformations: phenotypic dimorphisms N=2 absence of septum pellucidum N=1 sagittal craniosynostosis N=1 pulmonary peripheral stenosis N=1 hypospadias N=1 persistent pulmonary hypertension N=0 Unexposed: phenotypic dimorphisms N=3 angioma N=1 heart murmur N=1 cryptorchidia N=1	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Figueroa 2010[23] US Retrospective cohort Design/Data Source[AD] Medium	NR	ADHD by age of 5 years: (OR 95%CI) SSRI before pregnancy: 1.20 (0.70–2.04) P= .50 SSRI during pregnancy: 0.91 (0.51–1.60) P=.74 First trimester:1.62 (0.79–3.32) P=.19 Second trimester: .59 (0.58–4.35) P= .37 Third trimester: 0.38 (0.14–1.03) P=.06 SSRI after pregnancy: 2.04 (1.43–2.91) P<.001 Bupropion before pregnancy: 0.49 (0.12–2.02) P=.32 Bupropion during pregnancy: 3.63 (1.20–11.04) P=.02 First trimester: 2.06 (0.35–12.16) P=.42 Second trimester:14.66 (3.27–65.73) P<.001 Third trimester: <0.01 (<0.01–>99.9) P=.94 Bupropion after pregnancy: 0.90 (0.32–2.53) P=.84 Other antidepressant during pregnancy: 0.65 (0.09–4.79) P= .68 Anticonvulsants during pregnancy: 0.36 (0.05–2.65) P=.32 Benzodiazepines during pregnancy:1.82 (0.86–3.85) P=.12 Other psychotropics during pregnancy: <0.01 (<0.01–>99.9) P= .96	NR
Gorman, 2012[24] US, California Prospective cohort/TIS Medium	Exposed vs Unexposed: **Initiating breastfeeding:** SSRI Before delivery: Adjusted OR, 0.43; 95% CI, 0.20-0.94 SSRI At time of delivery: Adjusted OR 0.34; 95% CI, 0.16-0.72 Analysis by race, maternal age, alcohol use, low Apgar: NSD Cesarean birth 0.36 (0.20-0.66) Compared to high SES: Medium 0.46 (0.22-0.99) Low 0.23 (0.11-0.48) **Full breast-feeding at 2 weeks:** Before delivery 0.73 (0.41-1.32) At time of delivery 0.67 (0.39-1.15) Analysis by race, maternal age, BMI, SES = NSD	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Grzeskowiak 2012[25] Australia Retrospective cohort/LD Medium	(A) SSRI use vs psychiatric illness/no SSRI use (B) SSRI use vs no psychiatric illness Preterm delivery (<37 weeks): (A)=2.68 (1.83-3.93), (B) 2.46 (1.75-3.50) Low birth weight (<2500 g): (A)=2.26 (1.31-3.91), (B) 2.57 (1.57-4.21) SGA: (A)=1.13 (0.65-1.94), (B)=1.17 (0.71-1.94) Neonate admitted to hospital: (A)=1.92 (1.39-2.65), (B)=2.37 (1.76-3.19) Neonate length of stay > 3 days: (A)=1.93 (1.11-3.36), (B)=2.20 (1.34-3.59)	NR	NR
Heikkinen, 2002[26] Finland PC	Citalopram vs control Gestational age at birth (week) mean, range: 39 (37to 41) vs 40 (38to 41) Malformations: 0% vs 0% Weight at birth (g) mean (range): 3460 (2830to 4380) vs 3560 (3220 to 4260) Weight at 12 month (g), mean(range): 10560 (11810 to 9420) vs 9810 (10860 to 8900)	NR	Citalopram vs Control Delivery mode Vaginal: 91% vs 90% Cesarean: 9.1% vs 10% Breast-fed%: 81.8% vs 90%

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Jimenez-Solem 2012[27] Denmark RC-PD Low	Comparisons to women with no exposure, adjusted ORs (95% CI) First trimester/Paused during pregnancy Major malformations: 1.33 (1.16 to 1.53)/1.27 (0.91-1.78) Congenital malformations of the heart: 2.01 (1.60 to 2.53/1.85 (1.07-3.20) Septal defects: 2.04 (1.53-2.72)/2.56 (1.41-4.64) Ventricular septal defects: 1.62 (1.05-2.50)/3.74 (1.93-7.23) Atrial septal defects: 2.60 (1.84-3.68)/2.61 (1.17-5.84) Congenital malformations of the digestive system: 1.80 (1.04-3.12)/0.75 (0.11-5.35) Congenital malformations of the internal urinary system: 0.84 (0.45-1.57)/None Congenital malformations of the external genital organs: 1.55 (0.99-2.44)/0.89 (0.22-3.59) Congenital malformations of the limbs: 0.93 (0.71-1.23)/1.37 (0.80-2.32) Low-dose/high-dose SSRI during pregnancy Major malformations: 1.26 (1.05-1.51)/1.44 (1.15-1.79) Congenital malformations of the heart: 1.83 (1.35-2.48)/2.25 (1.60-3.19) Congenital malformations of the digestive system: 1.78 (0.89-3.58)/1.80 (0.75-4.35) Congenital malformations of the internal urinary system: 0.82 (0.37-1.83)/0.88 (0.33-2.34) Congenital malformations of the external genital organs: 1.32 (0.72-2.46)/1.91 (0.99-3.68) Congenital malformations of the limbs: 0.94 (0.67-1.33)/0.91 (0.59-1.42) Septal defects: 1.86 (1.15-3.00)/1.12 (0.28-4.51)/1.73 (0.89-3.33)/1.89 (0.85-4.23)/3.09 (1.82-5.25) When analyses were further adjusted for co-medications, the results showed no considerable change in the estimates or their level of significance. Individual SSRIs: citalopram/escitalopram/fluoxetine/paroxetine/sertraline Major: 1.51 (1.21-1.87)/0.69 (0.34-1.4)/1.18 (0.86-1.61)/1.25 (0.84-1.85)/1.41 (1.03-1.92) Of the nervous system: 0.84 (0.21-3.37)/2.25 (0.32-16.05)/1.44 (0.36-5.79)/1.19 (0.17-8.45)/0.85 (0.12-6.07) Neural tube defects: Only fluoxetine=3.22 (0.45-23.03) Of the eye: 2.62 (1.09-6.34)/None/0.93 (0.13-6.63)/None/1.05 (0.15-7.45) Of the ear, face and neck: None/None/None/8.32 (1.16-59.81)/6.13 (0.85-44.05) Of the heart: 1.91 (1.31-2.77)/1.06 (0.34-3.3)/2.05 (1.27-3.31)/1.54 (0.77-3.1)/2.73 (1.75-4.26)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Jimenez-Solem 2012[27] …….(CONT)	.....(CONT)..... Of the nervous system: 0.84 (0.21-3.37)/2.25 (0.32-16.05)/1.44 (0.36-5.79)/1.19 (0.17-8.45)/0.85 (0.12-6.07) Neural tube defects: Only fluoxetine=3.22 (0.45-23.03) Of the eye: 2.62 (1.09-6.34)/None/0.93 (0.13-6.63)/None/1.05 (0.15-7.45) Of the ear, face and neck: None/None/None/8.32 (1.16-59.81)/6.13 (0.85-44.05) Of the heart: 1.91 (1.31-2.77)/1.06 (0.34-3.3)/2.05 (1.27-3.31)/1.54 (0.77-3.1)/2.73 (1.75-4.26) Septal defects: 1.86 (1.15-3)/1.12 (0.28-4.51)/1.73 (0.89-3.33)/1.89 (0.85-4.23)/3.09 (1.82-5.25) Ventricular septal defects: 1.41 (0.67-2.96)/0/1.03 (0.33-3.2)/1.13 (0.28-4.54)/3.6 (1.86-6.96) Atrial septal defects: 2.41 (1.36-4.26)/1.01 (0.14-7.23)/2.53 (1.2-5.32)/3.51 (1.57-7.87)/2.85 (1.35-5.99) Atrioventricular septal: 0/8.71 (1.21-62.64)/0/0/3.22 (0.45-23.03) Of the respiratory system: 1.03 (0.26-4.11)/2.66 (0.37-19.02)/0.94 (0.13-6.67)/1.52 (0.21-10.8)/2.09 (0.52-8.38) Oro-facial clefts: 1.8 (0.67-4.81)/0/0.76 (0.11-5.4)/0/0.88 (0.12-6.24) Of the digestive system: 2.5 (1.19-5.27)/0/1.25 (0.31-5)/2.09 (0.52-8.39)/1.43 (0.36-5.74) Abdominal wall defects: 2.54 (0.35-18.3)/0/0/0/0 Of the internal urinary system: 2.02 (1.05-3.89)/0/0/0/0.44 (0.06-3.11) Of the external genital organs: 1.7 (0.85-3.41)/1.08 (0.15-7.67)/1.09 (0.35-3.38)/3.83 (1.71-8.57)/0.41 (0.06-7.93) Of the limbs: 1.13 (0.76-1.7)/0.25 (0.04-1.75)/0.76 (0.41-1.42)/0.91 (0.43-1.92)/1 (0.55-1.81) Of the musculoskeletal system: 1.25 (0.4-3.88)/2.18 (0.31-15.57)/1.46 (0.36-5.85)/1.2 (0.17-8.55)/0.83 (0.12-5.9) Chromosomal abnormalities: 0.59 (0.08-4.19)/0/0.97 (0.14-6.92)/4.65 (1.49-14.53)/2.35 (0.59-9.45) Other malformations: 1.32 (0.42-4.12)/0/3.08 (1.15-8.23)/0/0.88 (0.12-6.28)		
Jimenez-Solem 2012[27] …….(CONT)	(CONT) And teratogenic syndromes: 3.58 (0.49-26.33)/0/0/0/10.13 (1.36-75.44) Genetic syndromes: 0.39 (0.06-2.78)/0/1.79 (0.25-12.76)/0/0 Non-SSRI antidepressants: TCAs/other antidepressants: Any congenital malformation: 1.04 (0.53-2.03)/0.70 (0.47-1.05) Malformations of the heart: 1.33 (0.42-4.15)/0.99 (0.51-1.91)		

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Jimenez-Solem, 2013[28] Denmark PBR Low	Stillbirth/neonatal mortality, adjusted OR (95% CI) Unexposed: 1.00 (reference) Any SSRI 1st trimester: 0.77 (0.43,1.36)/0.56 (0.25,1.24) 1st and 2nd trimester: 0.84 (0.40,1.77)/0.90 (0.37, 2.17) All trimesters: 1.06 (0.71, 1.58)/1.27 (0.82, 1.99) Fluoxetine 1st trimester: 1.37 (0.56, 3.31)/1.18(0.38, 3.67) 1st and 2nd trimester: 0.65 (0.16, 2.63)/1.98 (0.74, 5.31) All trimesters: 0.97 (0.50, 1.87)/0.63 (0.24, 1.69) Citalopram 1st trimester: 0.60 (0.25, 1.45)/0.71 (0.27, 1.91) 1st and 2nd trimester: 0.26 (0.04, 1.88)/0.83(0.21, 3.32) All trimesters: 1.44 (0.74, 2.79)/2.49 (1.33, 4.65) Escitalopram 1st trimester: --/0.86 (0.12, 6.12) 1st and 2nd trimester: 1.29 (0.18, 9.28)/-- All trimesters: --/2.07 (0.29, 14.85) Paroxetine 1st trimester: 0.94(0.23, 3.78)/-- 1st and 2nd trimester: 2.28 (0.73, 7.17)/2.08 (0.52, 8.40) All trimesters: 0.66 (0.17, 2.67)/1.95 (0.73, 5.23) Sertraline 1st trimester: 1.05 (0.34, 3.28)/0.98 (0.24, 3.92) 1st and 2nd trimester: 0.54 (0.08, 3.87)/0.82(0.12, 5.85) All trimesters: 1.02 (0.46, 2.29)/0.26 (0.04, 1.81)	NR	NR
Jordan 2008 [29] US Clinic Appt Logs, Pediatrics records review AD Medium	HARMS: 28% SRI neonates: Newborn Behavioral Syndrome. No more likely to be admitted to NICU, have Resp abnormal, prolonged hosp	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Kallen, 2004[30] Sweden PBR Medium	ORs for type and timing of antidepressant use, vs. total population Preterm Delivery (<37 week) All antidepressants: OR, 1.96; 95%CI, 1.60 to 2.41 ≥24 week: OR, 2.02; 95%CI, 1.54 to 2.63 Tricyclic drugs: OR, 2.50; 95%CI, 1.87 to 3.34 SSRIs: OR, 2.06; 95%CI, 1.58 to 2.69 Low Birth Weight (<2500 g) All antidepressants: OR, 1.98; 95%CI, 1.55 to 2.52 ≥24 week: OR, 1.66; 95%CI, 1.18 to 2.34 Tricyclic drugs: OR, 1.88; 95%CI, 1.28 to 2.76 SSRIs: OR, 1.98; 95%CI, 1.42 to 2.76 Small for GA (≤2 SDs) All antidepressants: OR, 0.83; 95%CI, 0.53 to 1.30 ≥24 week: OR, 0.96; 95%CI, 0.56 to 1.65 Tricyclic drugs: OR, 1.00; 95%CI, 0.52 to 1.94 SSRIs: OR, 0.80; 95%CI, 0.44 to 1.44 Large for GA (≥2 SDs) All antidepressants: OR, 1.20; 95%CI, 0.93 to 1.56 ≥24 week: OR, 1.20; 95%CI, 0.85 to 1.70 Tricyclic drugs: OR, 1.18; 95%CI, 0.79 to 1.74 SSRIs: OR, 1.19; 95%CI, 0.83 to 1.70 Respiratory Distress All antidepressants: OR, 2.21; 95%CI, 1.71 to 2.86 ≥24 week: OR, 2.12; 95%CI, 1.50 to 3.00 Tricyclic drugs: OR, 2.20; 95%CI, 1.44 to 3.35 SSRIs: OR, 1.97; 95%CI, 1.38 to 2.83 Jaundice All antidepressants: OR, 1.13; 95%CI, 0.84 to 4.27	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Kallen, 2004 (Cont)[30]	CONTINUED..... ≥24 week: OR, 1.05; 95%CI, 0.70 to 1.59 Tricyclic drugs: OR, 1.37; 95%CI, 0.88 to 2.12 SSRIs: OR, 0.96; 95%CI, 0.63 to 1.46 Hypoglycemia All antidepressant: OR, 1.62; 95%CI, 1.22 to 2.16 ≥24 week: OR, 1.49; 95%CI, 1.00 to 2.23 Tricyclic drugs: OR, 2.07; 95%CI, 1.36 to 3.13 SSRIs 24 539 1.35 (0.90-2.03) Low Apgar Score All antidepressants: OR, 2.33; 95%CI, 1.49 to 3.64 ≥24 week: OR, 3.36; 95%CI, 2.05 to 5.49 Tricyclic drugs: OR, 2.99; 95%CI, 1.58 to 5.65 SSRIs: OR, 2.28; 95%CI, 1.27 to 4.10 RR for Convulsions vs. No antidepressants All antidepressants: RR, 4.7; 95%CI, 2.2 to 9.0 ≥24 week: RR, 4.4; 95%CI, 1.4 to 10.3 Tricyclic drugs: RR, 6.8; 95%CI, 2.2 to 16.0 SSRIs: RR, 3.6; 95%CI, 1.0 to 9.3 Crude ORs, Paroxetine vs. Other SSRIs Preterm delivery (<37 week): OR, 1.28; 95%CI, 0.57 to 2.67 Low birth weight (<2500 g): OR, 1.44; 95%CI, 0.40 to 4.24 Small for GA: OR, 0.90; 95%CI, 0.09 to 4.34 Large for GA: OR, 1.77; 95%CI, 0.70 to 4.11 Respiratory distress: OR,1.23; 95%CI, 0.44 to 3.05 Jaundice: OR, 0.87; 95%CI, 0.21 to 2.71 Hypoglycemia: OR, 0.83; 95%CI, 0.20 to 2.55 Convulsions: OR, 1.40; 95%CI, 0.03 to 15.70		

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Kallen 2007[31] Sweden Retrospective cohort/Data Source[PBR] Medium	Risk for congenital malformations*: (Adjusted OR**, 95% CI): Any SSRI: 0.89 (0.79–1.07) Fluoxetine: 0.85 (0.61–1.19) Citalopram: 0.94 (0.78–1.13) Paroxetine: 1.03 (0.76–1.38) Sertraline: 0.78 (0.61–1.00) Fluvoxamine: 1.05 (0.13–3.80)** Escitalopram: 0.91 (0.19–2.66)** *Adjustments were made for year of birth, maternal age, parity, smoking, and > 3 previous miscarriages **Risk ratios	NR	NR
Kallen 2008[32] Sweden Unclear/Data Source[PBR] Medium	PPHN: Maternal use of SSRI and PPHN in births after 34 completed weeks: (Adjusted Risk Ratio, 95% CI) 2.4, (1.2–4.3) Risk for an infant to have PPHN exposed SSRI during pregnancy: Exposed in early pregnancy (Adjusted Risk Ratio, 95% CI) All infants: 2.01 (1.00–3.60) >34 weeks: 2.38 (1.19–4.25) >37 weeks: 2.36 (1.08–4.78) Exposed in early pregnancy with known exposure also in late pregnancy: (Adjusted Risk Ratio, 95% CI) All infants: 2.91 (0.94–6.78) >34 weeks: 1.40 (3.57 1.16–8.33) >37 weeks:1.24 (3.70 1.01–9.48)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Kieler 2012[33] Nordic countries Retrospective cohort, PBD Medium	Small for gestational age (< 2 SDs of sex-specific mean birth weight: Exposed=3% vs not exposed=2.4%, P=NR Apgar score at 5 min: 0-6: Exposed=1.1% vs not exposed=0.6% 7-10: Exposed=61.0% vs not exposed=61.3%, P=NR Persistent pulmonary hypertension, adjusted OR (95% CI), comparison to not exposed: Late exposure: Any SSRI: 2.1 (1.5 to 3.0) Fluoxetine: 2.0 (1.0 to 3.8) Citalopram: 2.3 (1.2 to 4.1) Paroxetine: 2.8 (1.2 to 6.7) Sertraline: 2.3 (1.3 to 4.4) Escitalopram: 1.3 (0.2 to 9.5) Early exposure: Any SSRI: 1.4 (1.0 to 2.0) Fluoxetine: 1.3 (0.6 to 2.8) Citalopram: 1.8 (1.1 to 3.0) Paroxetine: 1.3 (0.5 to 3.5) Sertraline: 1.9 (1.0 to 3.6) Escitalopram: 0.3 (0.0 to 2.2)	NR	NR
Kornum, 2010[34] Denmark PBR Medium	Escitalopram (n=5): OR, 2.0; 95% CI, 0.8 to 4.9 Non-SSRI antidepressant (n=6): OR, 0.6; 95% CI, 0.3 to 1.3 Cardiac malformations: Any SSRI (n=26): OR, 1.7; 95% CI, 1.1 to 2.5 Fluoxetine (n=6): OR, 1.9; 95% CI, 0.8 to 4.3 Sertraline (n=7): OR, 3.0; 95% CI, 1.4 to 6.4 Paroxetine (n=1): OR, 0.5; 95% CI, 0.1 to 3.6 Citalopram (n=6): OR, 1.1; 95% CI, 0.5 to 2.7 Escitalopram (n=3): OR, 3.3; 95% CI, 0.8 to 13.4 Non-SSRI antidepressant (n=0) Septal heart defects: Any SSRI (n=18): OR, 1.4; 95% CI, 0.8 to 2.3 Fluoxetine (n=4): OR, 1.6; 95% CI, 0.6 to 4.4 Sertraline (n=6): OR, 3.3; 95% CI, 1.5 to 7.5 Paroxetine (n=1): OR, 0.7; 95% CI, 0.1 to 4.6 Citalopram (n=2): OR, 0.3; 95% CI, 0.0 to 2.1 Escitalopram (n=3): OR, 4.2; 95% CI, 1.0 to 17.1 Non-SSRI antidepressant (n=0)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Laine 2003[35] Finland Prospective cohort/Data Source[PC] Medium	Pregnancy and delivery outcomes: mean (SD) or median (range), exposed vs controls Duration of pregnancy (days): 274 (251-291) vs. 279 (254-289) Mode of delivery: (number of patients) Vaginal 16 vs 17 Cesarean 4 vs 3 Weight at birth 3455 g (457) vs 3534 g (438) Total infant weight at 2 months 5423g (476) vs 5458g (626) Full breastfeeding 9 weeks (0-43) vs 9 weeks (0-26) Total breastfeeding 17 weeks (0-52) vs 24 weeks (2-52)	NR	NR
Latendresse, 2011[36] U.S. PS Medium	Comparison to the unexposed OR, 95% CI: SSRI use and prediction of preterm birth 11.7 (2.2 to 60.7), p=0.004	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Lennestal, 2007[37] Sweden PBR Medium	ORs for Birth Outcomes for singleton births, vs. all deliveries in the register Preterm birth (<37 wk.) SNRI/NRI exposure: OR, 1.60; 95%CI, 1.19 to 2.15 SSRI exposure: OR, 1.24; 95%CI, 1.11 to 1.39 Low birth weight (<2500 g) SNRI/NRI exposure: OR, 1.12; 95%CI, 0.74 to 1.68 SSRI exposure: OR, 1.06; 95%CI, 0.92 to 1.23 Small for GA (≤2 SD) SNRI/NRI exposure: OR, 0.68; 95%CI, 0.37 to 1.24 SSRI exposure: OR, 0.99; 95%CI, 0.83 to 1.18 Large for GA (>2 SD) SNRI/NRI exposure: OR, 1.02; 95%CI, 0.70 to 1.49 SSRI exposure: OR, 1.14; 95%CI, 1.02 to 1.28 ORs/Relative Risks for Neonatal Diagnoses by exposure, vs. all deliveries in the registry Respiratory problems* SNRI/NRI exposure Early: OR, 1.39; 95%CI, 0.99 to 1.96 Late: RR, 2.01; 95%CI, 0.96 to 3.69 SSRI exposure Early: OR, 1.17; 95%CI, 1.03 to 1.23 Late: OR, 1.72; 95%CI, 1.41 to 2.11 Low Apgar score (<7 at 5 min) SNRI/NRI exposure Early: RR, 1.54; 95%CI, 0.74 to 2.84 Late: RR, 1.71; 95%CI, 0.21 to 6.17 SSRI exposure Early: OR, 1.35; 95%CI, 1.08 to 1.68 Late: OR, 2.22; 95%CI, 1.58 to 3.12 Hypoglycemia SNRI/NRI exposure Early: OR, 1.42; 95%CI, 1.00 to 1.99 Late: RR, 2.11; 95%CI, 1.01 to 3.89 SSRI exposure Early: OR, 1.17; 95%CI, 1.02 to 1.33 Late: OR, 1.32; 95%CI, 1.05 to 1.68 Neonatal convulsions SNRI/NRI exposure Early: RR, 0.71; 95%CI, 0.02 to 3.95 Late: RR, 4.55; 95%CI, 0.12 to 25.3 SSRI exposure Early: OR, 1.39; 95%CI, 0.85 to 2.26 Late: OR, 2.94; 95%CI, 1.34 to 5.58	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Levinson-Castiel, 2006[38] Israel PC, PBD Medium	Infants exposed to SSRI vs no SSRI Congenital anomalies: 5% vs 1.7%, p=0.60 Head circumference, cm, mean (SD): 34.0 (1.2) vs 34.1 (1.2), p=0.65 % of patients with NAS: 30% vs 0%, p<0.001 Symptoms of NAS High-pitched cry: 30% vs 0% Sleep disturbances: 35% vs 3% Exaggerated moro reflex: 0.5% vs 0% Tremor: 61.7% vs 18.3% Hypertonicity or myoclonus: 23% vs 1.7% Convulsions: 3% vs 0% Sweating: 1.7% vs 0% Fever: 1.7% vs 0% Autonomic nervous system: 6.7% vs 3.3% Tachypnea: 20% vs 0% GI disturbance: 56.7% vs 3.3% Mean duration of hospital stay for neonates with severe NAS (n=8) exposed to SSRI: 5.3 days	NR	NR
Lewis 2010[39] Australia PC-Clinic Medium	Unadjusted ORs (95% CI) for medication vs control Clinical range for low birth weight: 8.33 (1.11-62.67) Clinical range for prematurity: 4.51 (0.47-43.41) Birth means: Gestational age, weeks: 38.86 vs 39.86; P=0.005 Weight, g: 3273.65 vs 3671.19; P=0.010 Length, cm: 49.30 vs 51.44; P=0.001 Head circumference, cm: 34.10 vs 34.87, P=0.084 One month: Age (days): 31.05 vs 28.55, P=0.038 Weight, g: 4032.05 vs 4582.95, P=0.006 Length, cm: 53.34 vs 54.70, P=0.042 Head circumference, cm: 36.96 vs 37.64, P=0.089 Mean rates of change over 1 month: Change in weight (g d -1): 22.71 vs 31.81, P=0.02 Change in length (mm d -1): 1.26 vs 1.15, P=0.590 Change in head circumference (mm d-1): 0.84 vs 0.86, P=0.800	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Logsdon, 2011[40] US, Pennsylvania PC Medium	NR	NR	Inventory of Functional Status after Childbirth Scale: NSD between groups: p=0.0549 Significant interaction with time: All groups, M(SD): p<0.0001 2-week, 2.9 (0.4); 12-week, 3.2(0.3); 26-week, 3.2(0.2); 52-week, 3.5(0.4)

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Louik 2007[41] US CC	Adjusted ORs and 95% CI [Reference group-all women not exposed to any antidepressant] Any SSRI vs Fluoxetine vs Sertraline vs Paroxetine vs Citalopram vs No-SSRI antidepressant SSRIs in relation to outcomes previously reported to be associated with SSRI use Reference group-Women not exposed to any antidepressant Craniosynostosis: 0.8 (0.2 to 3.5) vs none vs 1.8 (0.2 to 14.9) vs 1.7 (0.2 to 14.4) vs none vs none Omphalocele: 1.4 (0.4 to 4.5) vs none vs 5.7 (1.6 to 20.7) vs none vs none vs 1.2 (0.2 to 9.3) Any cardiac defect: 1.2 (0.9 to 1.6) vs 0.9 (0.6 to 1.5) vs 1.5 (0.9 to 2.6) vs 1.4 (0.8 to 2.5) vs 0.7 (0.2 to 2.1) vs 0.8 (0.5 to 1.5) Conotruncal defects: 1.2 (0.6 to 2.1) vs 1.3 (0.5 to 3.2) vs 0.7 (0.2 to 3.3) vs 1.7 (0.6 to 5.1) vs none vs 0.8 (0.5 to 1.5) Right ventricular outflow tract obstruction defects: 2.0 (1.1 to 3.6) vs 1.0 (0.2 to 3.4) vs 2.0 (0.6 to 6.8) vs 3.3 (1.3 to 8.8) vs none vs 0.9 (0.2 to 3.8) Left ventricular outflow tract obstruction defects: 1.6 (0.9 to 2.9) vs 1.6 (0.6 to 4.0) vs 1.9 (0.6 to 5.8) vs 0.5 (0.1 to 3.9) vs 3.3 (0.7 to 16.0) vs 0.6 (0.1 to 2.4) Septal defects: 1.2 (0.8 to 1.8) vs 1.0 (0.5 to 2.2) vs 2.0 (1.2 to 4.0) vs 0.8 (0.3 to 2.2) vs 0.8 (0.2 to 4.0) vs 1.1 (0.6 to 2.4) SSRI in relation to outcomes not previously reported to be associated with SSRI use Cleft lip with or without cleft palate: 1.5 (0.9-2.5) vs 1.8 (0.8 to 3.8) vs 1.1 (0.3 to 3.8) vs 1.2 (0.4 to 3.6) vs 3.2 (0.9 to 11.9) vs 1.2 (0.2 to 9.3) Pyloric stenosis: 1.1 (0.6 to 1.8) vs 0.9 (0.4 to 2.1) vs 1.7 (0.7 to 4.1) 0.7 (0.2 to 2.6) vs 2.1 (0.4 to 10.4) vs 1.1 (0.5 to 3.1) Renal-collecting-system defects: 1.1 (0.7 to 1.9) vs 1.0 (0.5 to 2.3) vs 1.7 (0.7 to 4.2) vs 1.0 (0.3 to 3.3) vs 1.9 (0.4 to 8.8) vs 0.7 (0.2 to 3.2) Hypospadias: 1.2 (0.6 to2.2) vs 0.7 (0.2 to 2.4) vs 1.2 (0.4 to 4.2) vs 1.0 (0.3 to 3.3) vs 1.9 (0.4 to 8.8) vs 0.7 (0.3 to 2.4) Clubfoot: 2.2 (1.4 to 3.6) vs 0.8 (0.2 to 2.5) vs 2.4 (0.9 to 6.2) vs 5.8 (2.6 to 12.8) vs 2.7 (0.5 to 13.1) vs 1.0 (0.3 to 3.2)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Louik 2007[41] US CC (CONT…)	(CONT…) Cleft palate alone: 0.9 (0.4 to 2.0) vs 1.0 (0.3 to 3.5) vs none vs 1.5 (0.4 to 5.3) vs 2.3 (0.4 to 12.6) vs 0.9 (0.3 to 3.2) Undescended testis: 1.3 (0.7 to 2.5) vs 0.4 (0.1 to 2.6) vs none vs 2.8 (1.0 to 7.8) vs 3.1 (0.6 to 15.5) vs 0.7 (0.2 to 3.0) Neural-tube defects: 0.6 (0.2 to 1.4) vs none vs 0.8 (0.1 to 6.3) vs 3.3 (1.1 to 10.4) vs none vs 0.6 (0.1 to 2.4) Anal atresia: 1.9 (0.8 to 4.3) vs 1.4 (0.3 to 6.1) vs 4.4 (1.2 to 16.4) vs 1.0 (0.1 to 7.8) vs 3.0 (0.3 to 28.2) vs 2.2 (0.6 to 7.8) Diaphragmatic hernia: 1.8 (0.7 to 4.2) vs 2.0 (0.6 to 6.9) vs 1.5 (0.2 to 11.5) vs 1.2 (0.2 to 8.9) vs none vs 1.1 (0.3 to 5.1) Limb-reduction defects: 1.7 (0.9 to 3.4) vs 1.7 (0.5 to 5.7) vs 3.9 (1.1 to 13.5) vs 1.0 (0.1 to 8.3) vs 4.0 (0.5 to 33.9) vs 0.7 (0.7 to 5.2)		
Lund, 2009[42] Denmark PC Medium	Comparisons to women with no exposure, adjusted OR (95% CI) Preterm delivery: 2.02 (1.29 to 3.16) Birth weight<2500g: 0.63 (0.15-2.67) NICU admission:2.39 (1.69 to 3.39) Adjusted difference (95% CI) Gestational age, days: -4.5 (-6.2 to -2.8) Birth weight, g: 21 (-51 to 94) Head circumference: -0.0 (-0.2 to 0.2)	NR	NR
Malm, 2011[43] Finland TIS Low	Adjusted OR for risk of major congenital anomalies, any SSRI (n, offspring=6,976): Overall Congenital Anomalies: OR, 1.08; 95%CI, 0.96 to 1.22 CV Anomalies: All major CV anomalies: OR, 1.09; 95%CI, 0.90 to 1.32 Organ system-specific anomalies: CNS: OR, 1.03; 95%CI, 0.68 to 1.57 Neural tube defects: OR, 1.85; 95%CI, 1.07 to 3.20 Respiratory tract: OR, 0.61; 95%CI, 0.28 to 1.30 Cleft lip with or without cleft palate: OR, 0.62; 95%CI, 0.25 to 1.51 Cleft palate: OR, 1.18; 95%CI, 0.67 to 2.08 Digestive system: OR, 0.87; 95%CI, 0.54 to 1.38 Urogenital: OR, 1.09; 95%CI, 0.80 to 1.50 Musculoskeletal: OR, 0.96; 95%CI, 0.75 to 1.23 Omphalocele: OR, 0.47; 95%CI, 0.11 to 1.94 Craniosynostosis: OR, 1.53; 95%CI, 0.61 to 3.87	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
McFarland, 2011[44] US, Rhode Island PC Medium	NR	NR	NSD for SRI use on Maternal Fetal Attachment Scale total score, p<0.66
Merlob, 2009[45] Israel TIS Medium	SSRI vs. Controls Nonsyndromic congenital heart malformations: N= 8/235 (3.4%) vs. 1,083/67,636 (1.60%); p=0.023 Risk of mild congenital heart defects: RR, 2.17; 95% CI, 1.07 to 4.39)	NR	NR
Misri 2006[46] Canada PC-Clinic Medium	NR	Internalizing behaviors at age 4 years, ORs (95% CI): All exposed (including clonazepam) vs unexposed Maternal depression-controlled (parent/caregiver): Emotionally reactive: 1.73 (0.25-11.80)/0.56 (0.08-4.01) Anxious/depressed: Parent NR/2.70 (0.25-29.30) Somatic complaints: 0.18 (0.02-1.48)/Caregiver NR Withdrawn: 1.23 (0.09-17.40)/Caregiver NR Total internalizing problems: 0.99 (0.13-7.88/2.85 (0.26-31.20) Clinician's ratings: Irritability=0.65 (0.07-5.69), Withdrawal=2.45 (0.60-10.00), positivity=0.46 (0.10-1.98) Maternal anxiety-controlled (parent/caregiver): Emotionally reactive: 2.10 (0.33-13.40)/0.44 (0.06-3.19) Anxious/depressed: Parent NR/3.21 (0.31-33.70) Somatic complaints: 0.32 (0.06-1.84)/Caregiver NR Withdrawal: 1.74 (0.15-20.10)/Caregiver NR Total internalizing problems: 1.08 (0.15-7.89)/3.45 (0.32-36.80) Clinician's ratings: Irritability=0.64 (0.08-5.51), wd=2.43 (0.59-9.84), positivity=0.46 (0.11-1.93) SSRIs only vs SSRIs plus clonazepam: Maternal depression-controlled (parent/caregiver): Emotionally reactive: 1.63 (0.23-11.80)/8.00 (0.25-255.00) Anxious/depressed: 1.67 (0.17-16.70)/1.29 (0.13-12.90) Somatic complaints: 4.79 (0.36-64.50)/Caregiver NR Withdrawn: 2.26 (0.15-34.20)/Caregiver NR Total internalizing problems: 4.60 (0.36-57.90)/1.53 (0.15-15.60) Clinician's ratings: Withdrawal=0.89 (0.15-5.06), positivity=4.57 (0.65-31.90) >Maternal anxiety-controlled (parent/caregiver): Emotionally reactive: 1.46 (0.20-10.50)/6.00 (0.18-196.00) Anxious/depressed: 1.32 (0.14-12.60/1.57 (0.15-16.20) Somatic complaints: 4.09 (0.29-56.30)/Caregiver NR Withdrawn: 2.00 (0.13-29.80)/Caregiver NR Total internalizing problems: 3.28 (0.25-42.60)/1.99 (0.19-21.10) Clinician's ratings: Withdrawal=0.99 (0.17-5.69), positivity=5.59 (0.59-52.50)	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Misri 2010[47] Canada PC-Clinic Medium	NR	NR	Exposure to prenatal SSRIs and SNRIs was not a significant predictor of parenting stress at 3-months or 6-months: β (P) Model 1: -0.145 (0.209)/-0.024 (0.843) Model 2: -0.086 (0.438)/0.038 (0.743)
Mulder 2011[48] The Netherlands Prospective cohort/Data Source[PC] Medium	(control vs. previously exposed vs. exposed) Birth weight in grams: mean (SD) 3463 (444) vs. 3392 (561) vs. 3395 (584) % with delivery at < 37 weeks: 0% vs. 5.4% vs. 8.3% Weeks gestation at delivery: mean (SD) 40.0 (1.1) vs. 39.4 (1.9) vs. 39.1 (2.1)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Nakhai-Pour, 2010[49] Canada CC Low	Risk of spontaneous abortion (Adjusted OR) Duration of exposure during year before pregnancy vs. no exposure: 1 month., OR, 1.18; 95% CI, 0.95 to 1.45; 2-6 month., OR, 0.98; 95% CI, 0.80 to 1.21; >6 month., OR, 0.72; 95% CI, 0.54 to 0.95. Use from first day of gestation to index date vs. no use: OR, 1.68; 95% CI, 1.38 to 2.06 Class of antidepressant vs. no use: SSRI alone, OR, 1.61; 95% CI, 1.28 to 2.04; Tricyclic antidepressant alone, OR, 1.27; 95% CI, 0.85 to 1.91; Serotonin-norepinephrine reuptake inhibitor alone, OR, 2.11; 95% CI, 1.34 to 3.30; Other (serotonin modulators, monoamine oxidase inhibitors, tetracyclic perazino-azepines, dopamine and norepinephrine reuptake inhibitors), OR, 1.53; 95% CI, 0.86 to 2.72; Combined use of ≥ 2 classes of antidepressants, OR, 3.51; 95% CI, 2.20 to 5.61. Type of SSRI vs. no use: Paroxetine, OR, 1.75; 95% CI, 1.31 to 2.34; Sertraline, OR, 1.33; 95% CI, 0.85 to 2.08; Fluoxetine, OR, 1.44; 95% CI, 0.86 to 2.43; Citalopram, OR, 1.55; 95% CI, 0.89 to 2.68; Fluvoxamine, OR, 2.19, 95 CI, 0.79 to 6.08; Venlafaxine, OR, 2.11; 95% CI, 1.34 to 3.30; Combined use of ≥ 2 SSRIs, OR, 2.47; 95% CI, 0.62 to 9.83.	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Nordeng, 2012[50] Norway PBR Medium	Any malformation/Major malformation/CV malformation, Adjusted OR (95% CI) Nonexposed: Reference Prior-only group: 1.14 (0.86, 1.51)/1.12 (0.78, 1.62)/0.69 (0.31, 1.55) Any antidepressant: 1.09(0.74, 1.62)/0.96 (0.55, 1.69)/1.24 (0.55, 2.82) SSRIs: 1.22 (0.81, 1.84)/1.07 (0.60, 1.91)/1.51 (0.67, 3.43) Citalopram/escitalopram: 1.47 (0.88, 2.46)/0.99 (0.44, 2.25)/1.51 (0.48, 4.77) Sertraline: 0.93 (0.34, 2.53)/--/-- Paroxetine: 0.95 (0.30, 3.02)/1.70 (0.55, 5.63)/-- Fluoxetine: 2.17 (0.47, 5.06)/--/-- Preterm birth, Adjusted OR (95% CI) Prior-only group: 1.12 (0.84, 1.49) Any antidepressant during pregnancy: 1.21(0.87, 1.69) SSRI during pregnancy: 1.28 (0.90, 1.84) Depressive symptoms week 17: 1.13 (1.03, 1.25) Low birthweight, Adjusted OR (95% CI) Prior-only group: 0.93 (0.55, 1.58) Any antidepressant during pregnancy: 0.62 (0.33, 1.16) SSRI during pregnancy: 0.64 (0.32, 1.26) Depressive symptoms week 17: 1.12 (0.95, 1.32)	NR	NR
Nulman, 2002[83] Canada PC Medium	NR	Cognitive outcomes (at 15-71 months) of children of women who took tricyclic antidepressants or fluoxetine throughout pregnancy: No difference in global IQ between antidepressant groups or nondepressed comparison women as measured by either Bayley or McCarthy test), Children in the tricyclic antidepressant group scored slightly higher on the Reynell Developmental Language Scales, but all 3 groups scored within the normal range. Multiple regression analysis showed the duration of maternal depression was a significant negative predictor of McCarthy global cognitive index. Antidepressant drugs themselves did not predict cognitive achievement. Number of depressive episodes after delivery had a negative relationship with language scores. Treatment for maternal depression was a positive predictor for language development. No differences among the 3 groups across 9 temperament scales (P=0.83) or 3 behavioral scales (P=0.83) of the Child Behavior Checklist.	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Oberlander 2002[52] Canada Prospective cohort/Data Source [PC] Medium	(exposed vs. exposed vs. control) Birth age: mean (SE) 39.5 (37.3-42.0) vs. 39.6 (37.6-41.6) vs. 39.2 (37.0-41.6) Birth weight in grams: mean (SE) 3401 (2703-4270) vs. 3490 (2865-4240) vs.3485 (2690-4150) Head circumference: 34.3 (32-37) vs. 34.53 (uninterpretable in table 1) vs. 35.0 (38.5-32) Length: 51.84 (47-64) vs. 51.5(49-54.5) vs. 51.6(47-57)	NR	Breastfeeding: N= 17 vs. 13 vs. 20
Oberlander, 2006[53] Canada, British Columbia PBR Medium	Outcome Mean, Depressed, with SSRI vs. Depressed, No SSRI vs. Not depressed, No SSRI; Difference score (95% CI), Depressed, with SSRI vs. Depressed, No SSRI Birth Weight, g: 3397 vs. 3429 vs. 3453; Difference, -32; 95%CI, -1 to -64; p=0.05 GA: 38.8 vs. 39.1 vs. 39.2; Difference, -0.35; 95%CI, -0.2 to -0.45; p<0.001 Preterm birth (<37weeks): 0.090 vs. 0.065 vs. 0.059; Difference, 0 .02; 95%CI, 0.009 to 0.04; p<0.001 Birth Weight <10th %: 0.085 vs. 0.081 vs. 0.074; Difference, 0.0005; 95%CI, -0.01 to 0.02; p=0.51 Length of hospital stay, days: 3.31 vs. 2.88 vs. 2.76; Difference, 0.43; 95%CI, 0.12 to 0.74; p=0.007 Respiratory Distress: 0.139 vs. 0.078 vs. 0.074; Difference, 0.063; 95%CI, 0.042 to 0.079; p<0.001 Feeding Problems: 0.039 vs. 0.024 vs. 0.021; Difference, 0.015; 95%CI, 0.005 to 0.025; p=0.002 Jaundice: 0.094 vs. 0.075 vs. 0.079; Difference, 0.019; 95% CI, 0.003 to 0.034; Convulsions: 0.0014 vs. 0.0009 vs. 0.0011; p=0.64 Propensity Score Matching: only birth weight <10th % (Difference, 0.033; 95%CI, 0.007 to 0.059; p=0.02) and respiratory distress (Difference, 0.044; 95%CI, 0.013 to 0.077; p=0.006) remained significantly different.	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Oberlander, 2008 [55] Canada, British Columbia PC Medium	SRI Exposed vs. Not Exposed GA, weeks: 39.34 vs. 40.14, p<0.05 Birth weight, g: 3404.95 vs. 3605.94, NSD Small for GA: 3 vs. 1, NSD Apgar, 1 minute (M): 7.54 vs. 8.13, NSD, not moderated by SLC6A4 genotype. Apgar, 5 minutes (M): 8.70 vs. 9.06, p<0.05, significant interaction between SRI exposure and SLC6A4 genotype (F=3.28, P=0.043);	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Oberlander, 2008[55] (Birth Defects Res Part B) Canada, British Columbia PBR Medium	Adjusted risk differences, exposure group compared to no exposure group Major Congenital Anomalies, adjusted risk difference (95% CI) SRIs only: -0.61 (-1.44 to 0.21) SRIs + benzodiazepines: 1.65 (-0.49 to 3.79) CV Congenital Defects, adjusted risk difference (95% CI) SRIs only: 0.21 (-0.14 to 0.56) SRIs + benzodiazepines: 1.18 (0.18 to 2.18) Ventricular Septal Defects, adjusted risk difference (95% CI) SRIs only: 0.10 (-0.12 to 0.33) SRIs + benzodiazepines: 0.35 (-0.26 to 0.9) Atrial Septal Defects, adjusted risk difference (95% CI) SRIs only: 0.21 (0.05 to 0.36) SRIs + benzodiazepines: -0.01 (-0.31 to 0.30) SRI monotherapy Major Congenital Anomalies, adjusted risk difference (95% CI) Citalopram: 0.40 (-3.13 to 3.93) Fluoxetine: -0.26 (-1.68 to 1.17) Fluvoxamine: -1.52 (-4.02 to 0.98) Paroxetine: -0.56 (-1.70 to 0.59) Sertraline: -0.41 (-1.84 to 1.02) Venlafaxine: -1.18 (-3.20 to 0.84) SRI monotherapy CV Congenital Defects, adjusted risk difference (95% CI) Citalopram: 2.28 (0.19 to 4.36) Fluoxetine: 0.08 (-0.54 to 0.70) Fluvoxamine: -0.55 (-1.45 to 0.36) Paroxetine: 0.12 (-0.38 to 0.62) Sertraline: -0.09 (-0.65 to 0.47) Venlafaxine: 0.01 (-0.77 to 0.79)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Okun, 2011[56] US, Ohio and Pennsylvania PC Medium	NR	NR	Mean depression ratings: Hamilton Rating Scale for Depression, SSRI vs. No SSRI (depressed and non-depressed): Week 20: 6.6 vs. 5.1, p=0.01 Week 30: 6.5 vs. 4.1, p=0.0001 Week 36: 6.2 vs. 3.9, p=0.007 Hamilton Rating Scale for Depression, Atypical symptoms: Week 20: 4.0 vs. 3.6, p=0.27 Week 30: 4.2 vs. 3.4, p=0.04 Week 36: 4.0 vs. 3.4, p=0.07 Structured interview, Hamilton Rating Scale for Depression: Week 20: 10.5 vs. 8.7, p=0.03 Week 30: 10.6 vs. 7.5, p=0.0004 Week 36: 10.2 vs. 7.3, p=0.01 Atypical Symptoms/Structured interview, Hamilton Rating Scale for Depression: Week 20: 38.1 vs. 46.9, p=0.01 Week 30: 39.8 vs. 45.4, p=0.07 Week 36: 44.6 vs. 47.4, p=0.53
Okun, 2012[57] US, Ohio and Pennsylvania PC Medium	ORs for pre-term birth compared to No MDD, No SSRI group. Week 20 No MDD, taking SSRI: OR, 4.15; 95% CI, 1.43 to 12.0 MDD, No SSRI: OR, 1.45; 95% CI, 0.43 to 4.88 MDD, taking SSRI: OR, 3.76; 95% CI, 1.04 to 13.6 Week 30 No MDD, taking SSRI: OR, 7.93; 95% CI, 2.44 to 25.7 MDD, No SSRI: OR, 1.36; 95% CI, 0.27 to 6.94 MDD, taking SSRI: OR, 5.00; 95% CI, 1.42 to 17.5	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Palmsten 2012[58] Canada RC-LD Medium	NR	NR	Preeclampsia, adjusted RR vs unexposed (95% CI): SSRI monotherapy: 1.22 (0.97-1.54) SSRI polytherapy: 1.28 (0.73-2.22) SNRI monotherapy: 1.95 (1.25-3.03) TCA monotherapy: 3.23 (1.87-5.59) Preeclampsia, adjusted RR for continuation
Pearson 2007[59] US, Louisiana Retrospective cohort Data/Source: [AD] Medium	Adjusted for tobacco use, marital status, maternal age, parity.	Exposed vs. Not Exposed N=252 Birth weight: mean (SD) 3.28 (.48) vs. 3.3 (.63) Gestational age wk: mean (SD) 39 (1.7) vs. 38.9 (2.3) Premature delivery: 10.7% vs. 10.1% Caesarean section: 16.7% vs. 26.8% Admission to SCN: 17.9% vs. 10.1% Timely SCN discharge: 73.3 % vs. 10.1% Neonatal outcomes SRIs vs. TCAs: SRIs N=42, TCAs N=37 Low birth weight: 2.4% vs. 5.4% Prematurity: 7.1% vs. 16.2% Admission to SCN: 11.9% vs. 29.7% Timely SCN discharge: 80% vs. 63.6%	NR
Pedersen, 2009[60] Denmark PBD, LD Medium	Comparisons to unexposed infants, Adjusted OR (95% CI) Fluoxetine vs citalopram vs paroxetine vs sertraline vs >1 type of SSRI Minor malformations: 0.62(0.20 to 1.93) vs 0.79 (0.33 to 1.91) vs 1.43 (0.64 to 3.22) vs 0.76 (0.24 to 2.37) vs 1.08 (0.34 to 3.38) Cardiac malformations: 0.77 (0.19 to 3.11) vs 1.75 (0.78 to 3.93) vs 0.88 (0.22 to 3.55) vs 2.36 (0.97 to 5.72) vs 3.42 (1.40 to 8.34) Septal heart defects: 1.34 (0.33 to 5.41) vs 2.52 (1.04 to 6.10) vs 0.76 (0.11 to 5.43) vs 3.25 (1.21 to 8.75) vs 4.70 (1.74 to 12.7) Non-cardiac malformations: 1.08 (0.54 to 2.19) vs 0.83 (0.41 to 1.67) vs 1.59 (0.85 to 2.99) vs 1.18 (0.56 to 2.50) vs 0.95 (0.35 to 2.57)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Pedersen, 2010[61] Denmark PC Medium	6 month., Adjusted OR <u>Achievement of milestones, antidepressants vs. untreated depression</u> Head control OR, 1.0; 95% CI, 0.2 to 6.1; Sits with straight back OR, 2.2; 95% CI, 1.0 to 4.8; Rolls from back to belly OR, 1.5; 95% CI, 1.0 to 2.1; Sits without support OR, 1.2; 95% CI, 0.8 to 1.7; All motor activity OR, 1.3; 95% CI, 0.9 to 1.5; Throws things on floor OR, 1.7; 95% CI, 0.9 to 2.3; Tries to get things out of reach OR, 1.2; 95% CI, 0.4 to 3.5; Moves around OR, 1.3; 95% CI, 0.9 to 1.8; Puts toys in mouth OR, 0.7; 95% CI, 0.1 to 7.4; Looks after new sounds OR, 5.0; 95% CI, 0.6 to 44.8; Makes sounds when playing OR, 1.7; 95% CI, 0.3 to 10.2; Mimics new sounds OR, 1.3; 95% CI, 0.9 to 1.9; Tries to get into contact by sounds OR, 1.4; 95% CI, 0.8 to 2.5; Shows when not happy OR, 1.1; 95% CI, 0.6 to 1.9; Likes to get tossed around OR, 1.1; 95% CI, 0.6 to 2.0; All milestones OR, 1.5; 95% CI, 1.1 to 2.0 First- trimester antidepressants only vs. untreated depression Head control OR, 0.9; 95% CI, 0.1 to 7.3; Sits with straight back OR, 1.8; 95% CI, 0.7 to 4.6; Rolls from back to belly OR, 1.6; 95% CI, 1.0 to 2.4; Sits without support OR, 0.9; 95% CI, 0.8 to 1.7; All motor activity OR, 1.1; 95% CI, 0.7 to 1.8; Throws things on floor OR, 2.1; 95% CI, 1.0 to 4.4; Tries to get things out of reach OR, 1.9; 95% CI, 0.6 to 6.1; Moves around OR, 1.2; 95% CI, 0.8 to 1.7; Looks after new sounds OR, 4.4; 95% CI, 0.4 to 50.5; Makes sounds when playing OR, 1.5; 95% CI, 0.1 to 19.4; Mimics new sounds OR, 1.4; 95% CI, 0.8 to 1.9; Tries to get into contact by sounds OR, 1.4; 95% CI, 0.9 to 3.8; Shows when not happy OR, 0.8; 95% CI, 0.4 to 1.8; Likes to get tossed around OR, 0.8; 95% CI, 0.3 to 2.4; All milestones OR, 1.1; 95% CI, 0.6 to 2.1	19 month., Adjusted OR <u>Antidepressants vs. untreated depression</u> Going up stairs with support OR, 1.0; 95% CI, 0.50 to 2.05; Taking off socks and shoes when asked to OR, 1.1; 95% CI, 0.68 to 1.64; Drinking from ordinary cup without help OR, 3.4; 95% CI, 0.66 to 17.0; Being occupied alone for ≥15 min OR, 1.2; 95% CI, 0.72 to 1.87; Bringing things when told to OR, 0.8; 95% CI, 0.28 to 2.45; Making marks on table or paper OR, 1.3; 95% CI, 0.59 to 3.07; Aligning picture correctly OR, 1.0; 95% CI, 0.68 to 1.42; Using word-like sounds to tell what he or she wants OR, 1.4; 95% CI, 0.59 to 3.11; Mentioning ≥25 names of different things OR, 1.7; 95% CI, 0.95 to 3.10; Using 2-word sentences OR, 1.2; 9% CI, 0.83 to 1.74; Failed ≥1 milestone OR, 2.1 95%CI, 0.95 to 4.86 First- trimester antidepressants only vs. untreated depression Going up stairs with support OR, 1.4; 95% CI, 0.41 to 4.82; Taking off socks and shoes when asked to OR, 1.1; 95% CI, 0.65 to 2.0; Drinking from ordinary cup without help OR, 10.1; 95% CI, 0.20 to 512; Being occupied alone for ≥15 min OR, 0.9; 95% CI, 0.47 to 1.73; Bringing things when told to OR, 0.2; 95% CI, 0.03 to 1.42; Making marks on table or paper OR, 1.6; 95% CI, 0.58 to 4.40; Aligning picture correctly OR, 1.1; 95% CI, 0.71 to 1.83; Using word-like sounds to tell what he or she wants OR, 0.7; 95% CI, 0.20 to 2.56; Mentioning ≥25 names of different things OR, 1.2; 95% CI, 0.58 to 2.49; Using 2-word sentences OR, 1.0; 9% CI, 0.63 to 1.63; Failed ≥1 milestone OR, 2.3 95%CI, 0.72 to 7.49	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Pedersen, 2010[61] Denmark PC Medium (CONT…)	(Cont…) Second/Third-trimester antidepressants vs. untreated depression Sits with straight back OR, 2.7; 95% CI, 0.9 to 8.0; Rolls from back to belly OR, 1.4; 95% CI, 0.9 to 2.3; Sits without support OR, 2.1; 95% CI, 1.2 to 3.6; All motor activity OR, 2.2; 95% CI, 1.2 to 3.8; Throws things on floor OR, 1.3; 95% CI, 0.5 to 3.3; Tries to get things out of reach OR, 0.4; 95% CI, 0.0 to 3.2; Moves around OR, 1.5; 95% CI, 1.0 to 2.4; Mimics new sounds OR, 1.2; 95% CI, 0.7 to 2.1; Tries to get into contact by sounds OR, 1.3; 95% CI, 0.5 to 3.3; Shows when not happy OR, 1.4; 95% CI, 0.7 to 2.9; Likes to get tossed around OR, 1.1; 95% CI, 0.3 to 3.3; All milestones OR, 2.6; 95% CI, 1.2 to 5.8 6 months Sits Without Support Exposure at any point during pregnancy Antidepressants overall OR, 1.2; 95% CI, 0.83 to1.68; SSRIs overall OR, 1.1 95% CI, 0.76 to1.64; TCAs OR, 2.9; 95% CI, 0.89 to 9.51 First-trimester exposure only Antidepressants overall OR, 0.9; 95% CI, 0.78 to 1.74; SSRIs OR, 0.7; 95% CI, 0.45 to1.12; TCAs OR, 2.0; 95% CI, 0.58 to 6.91 Second/third-trimester exposure Antidepressants overall OR, 2.1; 95% CI, 1.23 to 3.60; SSRIs OR, 2.2; 95% CI, 1.25 to 3.89; TCAs NA (n=0)	(Cont…) Second/third trimester antidepressants vs. untreated depression Going up stairs with support OR, 0.6; 95% CI, 0.11 to 3.46; Taking off socks and shoes when asked to OR, 0.8; 95% CI, 0.45 to 1.53; Drinking from ordinary cup without help OR, 6.2; 95% CI, 0.39 to 98.0; Being occupied alone for ≥15 min OR, 2.1; 95% CI, 1.09 to 4.02; Bringing things when told to OR, 1.3; 95% CI, 0.29 to 5.79; Making marks on table or paper OR, 1.7; 95% CI, 0.52 to 5.76; Aligning picture correctly OR, 0.9; 95% CI, 0.56 to 1.55; Using word-like sounds to tell what he or she wants OR, 1.6; 95% CI, 0.59 to 4.38; Mentioning ≥25 names of different things OR, 2.3; 95% CI, 0.92 to 5.66; Using 2-word sentences OR, 1.6; 9% CI, 0.0.94 to 2.76; Failed ≥1 milestone OR, 2.3 95%CI, 0.72 to 7.49	

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Rai 2013[62] Sweden CC Low	NR	Adjusted OR (95% CI) Autism spectrum disorder Any antidepressant use: 1.90 (1.15-3.14) Any antidepressant use with depression: 3.34 (1.50-7.47) Any antidepressant use without depression: 1.61 (0.85-3.06) Depression and no antidepressant use: 1.06 (0.68 to 1.66) SSRIs: 1.65 (0.90-3.03) Nonselective MRIs: 2.69 (1.04-6.06) Autism spectrum disorder with intellectual disability Any antidepressant use: 1.09 (0.41-2.88) SSRIs: 1.01 (0.34-2.98) Nonselective MRIs: 1.72 (0.20-15.03) Any antidepressant use with depression: 1.81 (0.39-8.56) Any antidepressant use without depression: 0.93 (0.27-3.21) Depression and no antidepressant use: 1.06 (0.54 to 2.07) Autism spectrum disorder without intellectual disability Any antidepressant use: 2.54 (1.37-4.68) SSRIs: 2.34 (1.09-5.06) Nonselective MRIs: 2.93 (0.98-8.82) Any antidepressant use with depression: 4.94 (1.85-13.23) Any antidepressant use without depression: 2.10 (0.97-4.57) Depression and no antidepressant use: 1.04 (0.57-1.92)	NR
Ramos, 2008[84] Canada, Quebec LD Medium	Adjusted ORs for risk of major congenital malformations Timing of antidepressant exposure: First trimester: OR, 1.10; 95%CI, 0.75 to 1.62 Second trimester: OR, 1.13; 95%CI, 0.59 to 2.17 Third trimester: OR, 0.86; 95%CI, 0.45 to 1.65 Duration of antidepressant use during first trimester: 1–30 days: OR,1.23; 95%CI, 0.77 to 1.98 31–60 days: OR, 1.03; 95%CI, 0.63 to 1.69 ≥61 days: OR, 0.92; 95%CI, 0.50 to 1.69 Class of antidepressant used during first trimester: Paroxetine: OR, 1.27; 95%CI, 0.78 to 2.06 Other SSRI: OR, 1.19; 95%CI, 0.71 to 1.97 Tricyclic antidepressant: OR, 0.78; 95%CI, 0.30 to 2.02 Other antidepressant: OR, 0.94; 95%CI, 0.51 to 1.75 Co-exposure: OR, 1.03; 95%CI, 0.44 to 2.41	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Ramos, 2010[64] Canada, Quebec LD, supplemental questionnaire Medium	Adjusted Risk Ratio for Small for GA (birth weight <10th percentile) by Trimester and class of antidepressant vs. no antidepressants: First Trimester: SSRIs: RR, 0.96; 95%CI, 0.74 to 1.25 Tricyclics: RR, 0.84; 95%CI, 0.44 to 1.58 Other antidepressants: RR, 1.17; 95%CI, 0.83 to 1.66 Co-exposure: RR, 0.83; 95%CI, 0.51 to 1.35 Second Trimester: SSRIs: RR, 1.40; 95%CI, 0.96 to 2.02 Tricyclics: RR, 0.69; 95%CI, 0.18 to 2.60 Other antidepressants: RR, 2.25; 95%CI, 1.30 to 3.92 Co-exposure: RR, 3.48; 95%CI, 1.56 to 7.75 Third Trimester: SSRIs: RR, 0.70; 95%CI, 0.48 to 1.01 Tricyclics: RR, 2.12; 95%CI, 0.58 to 7.72 Other antidepressants: RR, 0.47; 95%CI, 0.24 to 0.90 Co-exposure: RR, 0.33; 95%CI, 0.12 to 0.89 Adjusted Risk Ratio for Small for GA by class of antidepressant used during the second trimester in subset of cohort (N=938) SSRIs: RR, 1.40; 95%CI, 0.73 to 2.67 Tricyclics: RR, 0.99; 95%CI, 0.13 to 7.37 Other antidepressants: RR, 2.41; 95%CI, 1.07 to 5.43 Co-exposure: RR, 3.28; 95%CI, 1.28 to 8.45	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Rampono, 2009[65] Australia PC Medium	Gestational age at delivery, Median (IQR): Cases: 39 (38-40) Controls: 40 (39-40) p<0.05 No significant differences for obstetric outcomes (labor, presentation or delivery mode) or neonatal outcomes (need for resuscitation, birth weight, or head circumference) Neonatal Abstinence: Present in 5% of cases (4% SSRIs, 9% venlafaxine) Maximum neonatal abstinence score on day 1, Median (IQR): Cases: 2 (0-1.05) Controls: 0 (0-6) P<0.05 No other differences in mean or maximum NAS scores (days 1-3 Brazelton Neonatal Behavioral Assessment Scale, Mean (SD): Controls/Cases/SSRI/SNRI (higher score indicates better response): Habituation: 7.64 (0.84)/6.57 (1.60)/6.62 (1.80)/6.46 (1.65) Social-interactive: 7.29 (1.12)/6.22 (1.90)/6.10 (2.02)/6.49 (1.63) Motor: 6.13 (0.44)/5.35 (0.59)/5.38 (0.55)/5.27 (0.69) Range: 3.53 (0.75)/3.49 (0.58)/3.47 (0.61)/3.55 (0.52) Regulation: 6.26 (1.00)/5.96 (1.18)/5.91(1.13)/6.09 (1.32) Autonomic: 6.20 (0.68)/5.51 (1.17)/5.52 (0.98)/5.47 (1.59) Reflexes: 0.75 (0.07)/0.73(0.09)/0.74 (0.08)/0.72 (0.11) P<0.05 for controls vs cases for habituation, social-interactive, and autonomic P<0.05 for controls vs SSRI vs SNRI for motor and autonomic	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Reebye, 2002[66] Canada PC Medium	SSRI vs SSRI+ vs nonexposed Bayley scale at 2 months Mental development index Mean (SD): 98 (8.1) vs 93 (5.1) vs 96 (7.5) Psychomotor development index Mean (SD): 106 (5.4) vs 102 (6.3) vs 101 (7.9) Gestational age, wks Mean (SD): 39.5(1.2) vs 39.5 (1.3) vs 39.3 (1.4) Birthweight, g Mean (SD): 3364 (408) vs 3515 (452) vs 3414 (437)	NR	SSRI alone vs SSRI plus vs Non-exposed Maternal infant positive correlations at 3 months During Feeding 0.35 vs 0.32 vs 0.58 (p<0.01) sensitivity: 0.40 (p<0.05) vs 0.06 vs -0.02 During free play 0.40 (p<0.05) vs 0.61(p<0.05) vs 0.20 sensitivity: 0.20 vs 0.51(p<0.05) vs -0.13 negativity: -0.26 vs -0.72 (p<0.05) vs -0.08 Intercorelations between parent variable and negative infant affect at 3 months SSRI Negative infant affect vs apathetic mood vs sober mood Feeding Positive maternal affect: -0.21 vs -0.17 vs 0.01 Free play Positive maternal affect: 0.04 vs -0.48 (p<0.05) vs -0.55 (p<0.05) Feeding sensitivity: -0.15 vs -0.08 vs -0.14 Free play sensitivity: -0.12 vs -0.38 (p<0.05) vs -0.17 Free play negativity: 0.25 vs 0.14 vs -0.05 SSRI + Negative infant affect vs apathetic mood vs sober mood Feeding Positive maternal affect:-0.57 (p<0.05) vs NR vs -0.26 Free play Positive maternal affect: -0.47 vs -0.23 vs -0.56 (p<0.05) Feeding sensitivity: 0.00 vs NR vs -0.33 Free play sensitivity: -0.15 vs -0.55(p<0.05) vs -0.43 Free play negativity: 0.53 (p<0.05) vs 0.38 vs 0.54 (p<0.05) Nonexposed: Negative infant affect vs apathetic mood vs sober mood Feeding Positive maternal affect: 0.35 vs -0.33 vs -0.39(p<0.05) Free play Positive maternal affect: -0.18 vs -0.55(p<0.05) vs -0.28 Feeding sensitivity: 0.30 vs 0.14 vs -0.28 Free play sensitivity: -0.15 vs -0.27 vs 0.18 Free play negativity: 0.17 vs 0.31 vs -0.6

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Reis, 2010[67] Sweden PBR Medium	Infant characteristics according to antidepressant use later in pregnancy: TCA/SSRI/SNRI, Adjusted OR (95% CI) Preterm birth (<37 weeks): 2.36 (1.89, 2.94)/1.46 (1.31, 1.63)/1.98 (1.49, 2.63) Low birthweight (<2500 gm): 1.39 (1.00, 1.95)/1.13 (0.97, 1.31)/1.87 (1.33, 2.64) High birthweight (>4500 gm): 0.62 (0.40, 0.95)/0.89 (0.70, 1.04)/0.80 (0.53, 1.38) Small for gestational age: 0.77 (0.45, 1.32)/1.01 (0.84, 1.22)/1.84 (1.20, 2.81) Large for gestational age: 1.12 (0.85, 1.48)/1.06 (0.93, 1.19)/1.23 (0.88, 1.72) Neonatal diagnoses in infants born after maternal antidepressant use: Early use/Later use/Both early and later use, Adjusted OR (95% CI) Hypoglycemia: 1.33 (1.22, 1.45)/1.43 (1.31, 1.65)/1.56 (1.36, 1.79) Respiratory diagnoses: 1.34 (1.25, 1.44)/1.62 (1.47, 1.79)/1.65 (1.46, 1.85) CNS diagnoses: 1.31 (1.11, 1.56)/1.50 (1.19, 1.88)/1.49 (1.013, 1.97) Jaundice: 1.09 (1.01, 1.19)/1.13 (1.01, 1.27)/1.22 (1.06, 1.39) Intracerebral hemorrhage: 1.17 (0.77, 1.78)/1.28 (0.66, 2.23)/1.20 (0.52, 2.37)	NR	Maternal delivery diagnoses after use of antidepressants: Early use/Later use/Both early and later use, Adjusted OR (95% CI) Preexisting diabetes: 1.35 (1.19, 1.52)/1.32 (1.11, 1.58)/-- Chronic hypertension: 1.34(1.18, 1.52)/1.25 (1.04, 1.51)/-- Gestational diabetes: 1.37 (1.18, 1.58)/1.16 (0.93, 1.45)/1.37 (1.08, 1.75) Pre-eclampsia: 1.28 (1.19, 1.37)/1.38 (1.25, 1.53)/1.50 (1.33, 1.69) Hyperemesis: 1.45 (1.27, 1.66)/1.31 (1.07, 1.60)/1.59 (1.28, 1.96) Placenta previa: 1.36 (1.20, 1.55)/1.21 (1.00, 1.47)/1.38 (1.11, 1.72) Placenta abruption: 1.29 (1.14, 1.47)/1.05 (0.86, 1.29)/1.23 (0.99, 1.53) Premature rupture of membranes: 1.30 (1.18, 1.43)/1.36 (1.19, 1.56)/1.47 (1.26, 1.72) Bleeding before partus: 1.25 (1.10, 1.42)/1.15 (0.95, 1.39)/1.34 (1.09, 1.66) Bleeding during partus: 1.33 (1.20, 1.46)/1.45 (1.27, 1.65)/1.58 (1.36, 1.84) Bleeding after partus: 1.11 (1.03, 1.19)/1.02 (0.92, 1.14)/1.08 (0.95, 1.22) Induction of delivery: 1.29 (1.22, 1.35)/1.29 (1.19, 1.38)/1.29 (1.18, 1.41) Caesarean section: 1.38 (1.32, 1.44)/1.35 (1.27, 1.44)/1.74 (1.30, 1.51)

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Salisbury, 2011[68] US, Rhode Island PC Medium	Non-MDD vs. MDD vs. MDD+SRI GA at birth: 39.48 vs. 39.66 vs. 38.99, F=3.6, p=0.03 Birth weight, g: 3,553.82 vs. 3,466.95 vs. 3,320, F=2.3, p=0.11 1 min-APGAR, % <8: 10.71% vs. 16.67% vs. 30.57%, x2=5.6, p=0.03 5 min-APGAR, %<9: 5.36% vs. 5.56% vs. 16.67%, x2 3.2, x2= 3.2, p=0.23 NICU network neurobehavioral scores, Non-MDD vs. MDD vs. MDD+SRI; Attention: 5.84 vs. 4.36 vs. 5.96, p=0.00 Quality of Movement: 4.63 vs. 4.82 vs. 4.27, p=0.05 Self-regulation: 5.50 vs. 5.47 vs. 5.27, p=0.67 Handling: 0.38 vs. 0.40 vs. 0.42, p=0.41 Arousal: 4.27 vs. 4.20 vs. 4.04, p=0.03 Excitability: 3.55 vs. 3.17 vs. 3.67, p=0.73 Lethargy: 3.02 vs. 4.24 vs. 3.34, p=1.00 Stress/abstinence signs, total: 0.08 vs. 0.08 vs. 0.11, p=0.10 Stress/abstinence signs, CNS: 0.05 vs. 0.0 vs. 0.13, p=0.00 Nonoptimal reflexes: 1.60 vs. 1.73 vs. 2.17, p=0.41 Asymmetrical reflexes: 0.33 vs. 0.50 vs. 0.56, p=0.72 Hypertonia: 0.05 vs. 0.04 vs. 0.16, p=0.05 Hypotonia: 0.16 vs. 0.05 vs. 0.23, p=0.49	NR	NR
Salkeld 2008[69] Canada CC-LD Low	NR	NR	Postpartum hemorrhage, multivariate OR (95% CI): 90-day exposure: SSRI: 1.30 (0.98–1.72) Non-SSRI: 1.12 (0.62–2.01) 30-day exposure: SSRI: 1.33 (0.94–1.89) Non-SSRI: 1.29 (0.58–2.84) 60-day exposure: SSRI: 1.40 (1.04–1.88) Non-SSRI: 1.11 (0.55–2.22) 180-day exposure: SSRI: 1.32 (1.03–1.70) Non-SSRI: 1.04 (0.61–1.75)

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Simon 2002[70] U.S. RC-HCDB Low	Exposed vs unexposed: Adjusted difference (95% CI): Estimated gestational age (weeks): TCAs= -0.2 (-0.6 to 0.2); SSRIs= -0.9 (–1.3 to –0.5); SSRIs in 3rd trimester only= –0.7 (–1.3 to –0.1); SSRIs in 1st or 2nd trimesters only= –0.9 (–1.5 to –0.4) Birth weight (g): TCAs= -53 (–167 to 62); SSRIs= -172 (–299 to –46); SSRIs in 3rd trimester only= –148 (–343 to 48); SSRIs in 1st or 2nd trimesters only= –169 (–336 to –2) Head circumference (cm): TCAs= 0.0 (–0.5 to 0.4); SSRIs= 0.0 (-1.0 to 1.0) Adjusted OR (95% CI): Estimated gestational age ≤ 36 weeks: TCAs= 1.86 (0.83 to 4.17); SSRIs= 4.38 (1.57 to 12.22) Birth weight <2500 g: TCAs= 1.18 (0.42 to 3.28); SSRIs= 2.73 (0.92 to 8.09) Major malformation: TCAs=0.82 (0.35 to 1.95); SSRIs=1.36 (0.56 to 3.30) Minor malformation: TCAs=0.76 (0.37 to 1.58); SSRIs=1.14 (0.56 to 2.31) Genitourinary malformation: TCAs=0.66 (0.23 to 1.88); SSRIs=1.17 (0.39 to 3.56) Cardiac malformation: TCAs=0.50 (0.05 to 5.53); SSRIs=NA (0 events in unexposed) Skeletal malformation: TCAs=0.80 (0.21 to 3.0); SSRIs=0.24 (0.05 to 1.15) Vascular malformation: TCAs=1.34 (0.30 to 6.06); SSRIs=1.15 (0.41 to 3.23) Craniofacial malformation: TCAs=1.26 (0.33 to 4.75); SSRIs=0.59 (0.14 to 2.52) Seizure disorder: TCAs=NA (0 events in unexposed): SSRIs=4.07 (0.45 to 36.73) Motor delay: TCAs=1.00 (0.14 to 7.17); SSRIs=1.1 3.07 (0.61 to 15.40) Speech delay: TCAs=1.00 (0.14 to 7.17); SSRIs=1.00 (0.14 to 7.18) Other motor abnormality: TCAs=0.49 (0.09 to 2.73); SSRIs=0.50 (0.09 to 2.73)	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Sit, 2011[71] US, Pennsylvania PC Medium	OR for Preterm Birth by Maximum depression level: OR, 1.0; 95%CI, 0.8 to 1.2 ORs for Infant Peripartum Events identified on Peripartum Events Scale by Maximum depression level: > 1 peripartum event: OR, 1.0; 95% CI, 0.8 to 1.2 ≥1 peripartum event: OR, 1.0; 95%CI, 0.9 to 1.2	NR	NR
Stephansson, 2013[72] Sweden PBR Medium	Exposure to SSRIs from 3 months before pregnancy until birth, adjusted OR (95% CI) Stillbirth: 1.17 (0.96, 1.41); P=0.12 Stillbirth, no previous psychiatric hospitalization: 1.07 (0.84, 1.36); P=0.59 Stillbirth, previous psychiatric hospitalization: 0.92 (0.66, 1.28); P=0.62 Neonatal death: 1.23 (0.96, 1.57); P=0.11 Neonatal death, no previous psychiatric hospitalization: 1.14 (0.84, 1.56); P=0.39 Neonatal death, previous psychiatric hospitalization: 0.89 (0.58, 1.39); P=0.62 Postneonatal death (28-364 days): 1.34(0.97, 1.86); P=0.08 Postneonatal death, no previous psychiatric hospitalization: 1.10 (0.71, 1.72); P=0.66 Postneonatal death, previous psychiatric hospitalization: 1.02 (0.61, 1.69); P=0.95 Exposure to SSRIs per trimester, adjusted OR (95% CI) Stillbirth/Neonatal death/Postneonatal death Unexposed: 1.0 (reference) T0: 1.19 (0.87, 1.65); P=0.28/1.04 (0.66, 1.64); P=0.86/1.28 (0.72, 2.26); P=0.40 T0-T1: 1.56 (1.06, 2.30); P=0.03/1.16 (0.61, 2.21); P=0.65/1.02 (0.42, 2.46); P=0.96 T0-T2: 1.11 (0.50, 2.48); P=0.80/1.135 (0.51, 3.62); P=0.55/2.06 (0.66, 6.39); P=0.821 T0-T3: 0.94 (0.53, 1.65); P=0.83/1.56 (0.86, 2.83); P=0.14/1.76 (0.79, 3.93); P=0.17 Other: 1.01 (0.70, 1.46); P=0.94/1.31 (0.85, 2.02); P=0.22/1.31 (0.72, 2.37); P=0.38	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Suri, 2007[73] US, California PC Medium	Birth Outcome Means (unless otherwise specified) by antidepressant use, MDD, with antidepressants vs. MDD, no antidepressants vs. No psychiatric history, no antidepressants: GA, weeks: 38.5 vs. 39.4 vs. 39.7; F=6.0, p=0.004 Birth weight, kg: 3.28 vs. 3.39 vs. 3.36; F=0.47, p=0.63 Apgar, 1 minute: 7.7 vs. 8.2 vs. 8.0; F=1.2, p=0.32 Apgar, 5 minute: 8.8 vs. 9.0 vs. 8.9; F=1.7, p=0.02 Preterm birth: 14.3% vs. 0% vs. 5.3%: $\chi 2$=6.0, p=0.05 Special care nursery: 21% vs. 9% vs. 0%; $\chi 2$=1.8, p=0.40 Birth Outcome Means (unless otherwise specified) by Antidepressant Dose, High vs. Low-Medium vs. None: GA, weeks: 38.2 vs. 38.8 vs. 39.5; F=3.1, p=0.05 Birth weight, kg: 3.29 vs. 3.30 vs. 3.38; F=0.17, p=0.85 Apgar, 1 minute: 7.3 vs. 8.0 vs. 8.1; F=1.9, p=0.16 Apgar, 5 minute: 8.7 vs. 8.9 vs. 8.9; F==0.82, p=0.44 Preterm birth: 20% vs. 9% vs. 0%; $\chi 2$=4.3, p=0.12 Special care nursery: 26.7% vs. 17.1% vs. 7.1%; $\chi 2$=2.1, p=0.36	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Suri, 2011[74] US, California PC Medium	Delivery Outcomes, MDD with antidepressants vs. MDD no antidepressants vs. No MDD GA, M weeks: 38.1 vs. 39.2 vs. 39.1; F=5.33, p<0.01 Preterm birth <37 weeks: 12% vs. 0% vs. 7%; F=3.34, p=0.19 Birth weight, kg: 3.3 vs. 3.4 vs. 3.3; F=0.46, p=0.63 Apgar, 1 minute, M: 7.8 vs. 8.2 vs. 8.0; F=0.75; p=0.48 Apgar, 5 minute, M: 8.8 vs. 8.9 vs. 9.0; F=1.83, p=0.17 Special care nursery, 18% vs. 12% vs. 0%; $\chi 2$=4.88, p=0.09 Brazelton Neonatal Behavioral Assessment Scale, Mean scores, MDD with antidepressants vs. MDD no antidepressants vs. No MDD 1 Week of Age: Habituation: 5.90 vs. 7.1 vs. 6.06; F=0.58, p=0.56 Orientation: 4.68 vs. 4.84 vs. 5.01; F= 0.12, p=0.88 Motor: 5.15 vs. 5.31 vs. 5.03; F=0.51, p=0.61 Regulation of state: 5.39 vs. 5.67 vs. 4.61; F=2.12, p=0.13 Range of state: 3.29 vs. 3.68 vs. 3.47; F=0.79, p=0.46 Rapidity of buildup: 2.33 vs. 3.75 vs. 3.18; F=3.28, p=0.05, but NSD after Bonferroni correction Autonomic stability: 7.06 vs. 6.76 vs. 7.41; F=1.29, p=0.28 Reflexes: 2.32 vs. 1.86 vs. 1.86; F=0.70; p=0.50 6-8 Weeks of Age: Habituation: 6.04 vs. 4.50 vs. 8.75; F=2.16, p=0.16 Orientation: 6.17 vs. 6.87 vs. 6.84; F=1.17, p=0.32 Inanimate auditory: 4.93 vs. 6.10 vs. 6.64; F=4.35, p=0.02, but NSD after Bonferroni correction Motor: 5.89 vs. 6.20 vs. 5.94; F=0.97, p=0.39 Defense: 7.19 vs. 7.00 vs. 6.31; F=3.39, p=0.04, but NSD after Bonferroni correction Range of state: 3.14 vs. 3.25 vs. 3.42; F=0.38, p=0.68 Autonomic stability: 7.48 vs. 7.67 vs. 7.61; F=0.31, p=0.74 Reflexes: 3.13 vs. 2.46 vs. 1.92; F=1.65, p=0.20	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Toh, 2009[75] US CC Medium	NR	NR	Any gestational hypertension, Adjusted RR (95% CI) No SSRI exposure: Reference SSRI exposure: 1.90 (1.35, 2.67) Discontinued SSRI exposure: 1.33 (0.78, 2.27) Continued SSRI exposure: 2.49 (1.62, 3.83) Gestational hypertension with preeclampsia, Adjusted RR (95% CI) SSRI exposure: 3.16 (1.89, 5.29) Discontinued SSRI exposure: 1.37 (0.50, 3.76) Continued SSRI exposure: 4.86 (2.70, 8.76) Gestational hypertension without preeclampsia, Adjusted RR (95% CI) SSRI exposure: 1.36 (0.85, 2.15) Discontinued SSRI exposure: 1.30 (0.69, 2.46) Continued SSRI exposure: 1.41 (0.74, 2.69)

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Ververs, 2009[76] the Netherlands AD Medium	RRs, Healthcare utilization, vs. non-users >First 2 Weeks of Life GP visits, ≥1 Continuous: RR, 0.9; 95%CI, 0.5 to 1.6 Irregular: RR, 0.9; 95%CI, 0.7 to 1.4 Stoppers: RR, 1.3 ; 95%CI, 0.9 to 1.6 >Specialist visits, 1 Continuous: RR,1.3; 95%CI, 1.1 to 1.5 Irregular: RR, 1.2; 95%CI, 1.0 to 1.3 Stoppers: RR, 0.9 ; 95%CI, 0.8 to 1.1 >Specialist visits, ≥2 Continuous: RR, 2.4; 95%CI, 1.7 to 3.3 Irregular: RR, 0.8; 95%CI, 0.6 to 1.2 Stoppers: RR, 1.1; 95%CI, 0.8 to 1.4 >Specialist procedures, 1 Continuous: RR, 1.5; 95%CI, 1.2 to 1.8 Irregular: RR, 1.1; 95%CI, 1.0 to 1.3 Stoppers: RR, 0.9; 95%CI, 0.8 to 1.1 >Specialist procedures, ≥2 Continuous: RR, 1.7; 95%CI, 1.1 to 2.6 Irregular: RR, 1.2; 95%CI, 0.9 to 1.6 Stoppers: RR, 0.8 ; 95%CI, 0.5 to 1.1 >Diagnostic tests, 1 Continuous: RR, 1.1; 95%CI, 0.8 to 1.6 Irregular: RR, 1.1; 95%CI, 0.9 to 1.3 Stoppers: RR, 1.1; 95%CI, 0.9 to 1.3	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Ververs, 2009[76] …….(CONT)	>Diagnostic tests, ≥2 Continuous: RR, 1.9; 95%CI, 1.4 to 2.5 Irregular: RR, 1.5; 95%CI, 1.2 to 1.9 Stoppers: RR, 0.9; 95%CI, 0.7 to 1.1 >Hospital admissions, 1 Continuous: RR,1.5; 95%CI,1.3 to 1.8 Irregular: RR, 1.2; 95%CI, 1.0 to 1.3 Stoppers: RR,1; 95%CI, 0.9 to 1.1 >Hospital admissions, ≥2 Continuous: RR,2.4; 95%CI, 1.8 to 3.1 Irregular: RR,1.4; 95%CI, 1.1 to 1.8 Stoppers: RR,0.8; 95%CI, 0.6 to 0.9 Drug prescriptions, ≥1 Continuous: RR, 0.5; 95%CI, 0.3 to 0.8 Irregular: RR, 0.9; 95%CI, 0.8 to 1.1 Stoppers: RR, 1; 95%CI, 0.9 to 1.2 First year of Life GP visits, 1 Continuous: RR, 1.0; 95%CI, 0.8 to 1.4 Irregular: RR, 1.0; 95%CI, 0.9 to 1.2 Stopper: RR, 1.1; 95%CI, 0.9 to 1.2 GP visits, ≥2 Continuous: RR, 1.5; 95%CI, 1.3 to 1.8 Irregular: RR, 1.2; 95%CI, 1.1 to 1.4 Stopper: RR, 1.3; 95%CI, 1.2 to 1.5		

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Ververs, 2009[76] …….(CONT)	Specialist visits, 1 Continuous: RR, 1.4; 95% CI, 1.1 to 1.8 Irregular: RR, 1.1; 95%CI, 0.9 to 1.3 Stopper: RR, 1.0; 95%CI, 0.9 to 1.2 Specialist visits, ≥2 Continuous: RR, 1.5; 95%CI, 1.2 to 1.9 Irregular: RR, 1.4; 95%CI, 1.2 to 1.6 Stopper: RR, 1.2; 95%CI, 1.1 to 1.4 Specialist procedures, 1 Continuous: RR, 1.6; 95%CI, 1.3 to 2.0 Irregular: RR, 1.1; 95%CI, 0.9 to 1.2 Stopper: RR, 1.1; 95%CI, 0.9 to 1.3 Specialist procedures, ≥2 Continuous: RR, 1.3; 95%CI, 0.9 to 1.7 Irregular: RR, 1.3; 95%CI, 1.1 to 1.5 Stopper: RR, 1.1; 95%CI, 0.9 to 1.3 Diagnostic tests, 1 to 2 Continuous: RR, 1.2; 95% CI, 0.9 to 1.6 Irregular: RR, 1.2; 95%CI, 0.9 to 1.4 Stopper: RR, 1.2; 95%CI, 0.9 to 1.4 Diagnostic tests, ≥3 Continuous: RR, 1.2; 95%CI, 0.8 to 1.6 Irregular: RR, 1.1; 95%CI, 0.9 to 1.4 Stopper: RR, 1.1; 95%CI, 0.9 to 1.3 Hospital admissions, 1 Continuous: RR, 2.2; 95%CI, 1.5 to 3.1 Irregular: RR, 1.1; 95%CI, 0.8 to 1.5		
Wen 2006[77] Canada RC, PBD Medium	SSRI exposed vs unexposed Adjusted difference (95% CI) Birth weight<2500g 1.58 (1.19 to 2.11) Gestational age<37 wk: 1.57 (1.28 to 1.92) Major structural anomalies: 0.98 (0.59 to 1.64) Minor structural anomalies: 1.02 (0.69 to 1.51) Fetal death: 2.23 (1.01 to 4.93) Infant death: 1.96 (0.97 to 3.94) Sepsis: 1.41 (0.65 to 3.06) Seizures: 3.87 (1.00 to 14.99) Mechanical ventilation: 1.14 (0.74 to 1.75)	NR	Preeclampsia: 1.20 (0.90 to 1.61) Urinary infection: 1.53 (0.76 to 3.09) Gestational diabetes mellitus: 1.31 (0.86 to 2.01) Placental previa: 1.20 (0.55 to 2.60) Placental abruption: 1.56 (0.99 to 2.46)

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Wilson, 2011[78] US CC Medium	PPHN, Adjusted OR (95% CI) Use of SSRI after 20 weeks: 0 (0, 3.0)	NR	NR
Wisner, 2009[79] US, Ohio Prospective cohort Medium	Minor physical anomalies Data available for 203 (85%) of infants. Neither first-trimester nor continuous exposure to SSRIs or depression was associated with a significant increase in the number of minor anomalies or the proportion of infants with three or more anomalies. No major malformations were observed. Infant birth weight Adjusted P = 012 across groups, Proportion < 10th or above 90th percentile, head circumference or length = NSD (P not given) Mean Weight (18), Kg sd No SSRI, no depression (N = 130) 3.53, 0.5 Continuous SSRI exposure (N = 47) 3.36, 0.7 Continuous depression, no SSRI (N = 14) 3.22, 0.6 Partial SSRI exposure (N = 22) 3.39, 0.4 Partial depression, no SSRI (N = 22) 3.37, 0.6 Gestational Age: p=0.08 across groups Preterm Birth; p=0.009. across groups Adjusted Rate Ratios Continuous SSRI exposure (N=48) 5.43 1.98–14.84 Continuous depression, no SSRI (N=14) 3.71 0.98–14.13 Partial SSRI exposure (N=23) 0.86 0.11–6.92 Partial depression, no SSRI (N=22) 1.04 0.22–5.01 NICU admissions p=0.88 across groups Score > 2 on Infant Subscale of Peripartum Events Scale: p=0.39 across groups; Post hoc Fisher's exact test indicated that the group with continuous SSRI exposure and the group with continuous depression and no SSRI exposure did not differ from each other and that both differed from the group with neither exposure.	NR	**Weight gain:** Adjusted P = 0.41 across groups Mean Weight gain (N), pounds, sd No SSRI, no depression (N = 82) 31.6, 13.0 Continuous SSRI exposure (N = 23) 28.6, 13.8 Continuous depression, no SSRI (N = 3) mean 17.7lbs, SD 15.5 Partial SSRI exposure (N = 16) 31.4, 12.0 Partial depression, no SSRI (N = 18) mean 24.8, SD 16.2

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Wogelius, 2006[80] Denmark PBR Medium	Congenital malformations, Adjusted OR (95% CI) Women who redeemed a prescription for an SSRI during 2nd and 3rd trimester All births: 1.34 (1.00, 1.79) >=37 weeks gestation: 1.23 (0.88, 1.72) <37 weeks gestation: 1.63 (0.85, 3.15) Women who redeemed a prescription for an SSRI during 1st trimester or 30 days before All births: 1.84 (1.25, 2.71) >=37 weeks gestation: 1.75 (1.14, 2.70) <37 weeks gestation: 1.77 (0.73, 4.32)	NR	NR
Yonkers 2012[81] US Prospective Cohort [PC] Low	Risk of preterm birth: (term vs. preterm) Additionally Adjusted OR and 95% CI Major depressive episode, exposed 1.51 (0.60-3.8) Major depressive episode, unexposed .86 (0.44-1.7) No major depressive episode, exposed 1.50 (0.94-2.4) No major depressive episode, unexposed reference category Risk of early and late preterm birth: (term vs. preterm) Adjusted OR and 95% CI Early preterm birth N=59 Major depressive episode, exposed NA Major depressive episode, unexposed 0.86 (0.29-2.6) No major depressive episode, exposed 0.93 (0.35-2.4) No major depressive episode, unexposed reference category Late preterm birth N=166 Major depressive episode, exposed 3.14 (1.5-6.8) Major depressive episode, unexposed 1.34 (0.71-2.5) No major depressive episode, exposed 1.93 (1.2-3.2) No major depressive episode, unexposed reference category	NR	NR

Author, year Country Study Design/Data source Risk of Bias	7. Fetus/infant/child outcomes up to 12 months of age	8. Child outcomes after 12 months of age	9. Maternal Outcomes
Zeskind 2004[82] US Prospective cohort study/Data Source [PC, AD] Medium	Gestational age, wk 38.66 (0.35) vs. 39.65 (0.20) P=.019 Birth weight, g 3453.53 (98.87) vs. 3297.35 (88.79) P=.25 Length, cm 51.06 (0.65) vs. 50.81 (0.43) P=.75 Head circumference, cm 33.87 (0.40) vs. 33.53 (0.40) P=.55 Neurobehavioral Outcomes: Adjusted Mean (SE) Tremulousness 2.32 (0.20) vs. 1.80 (0.20) P=0.038 Behavioral states: Number different: 2.53 (0.32) vs. 3.71 (0.32) P=0.009 Number of changes:7.15 (2.34) vs. 16.56 (2.34) P=0.005 Active sleep Number of epochs: 94.66 (6.64) vs. 83.46 (6.64) P=0.13 Number of bouts: 3.36 (0.44) vs. 6.58 (0.44) P=0.001 Longest bout: 68.20 (6.37) vs. 49.80 (6.37) P=0.03 Number of startles: 14.59 (2.70) vs. 9.85 (2.59) P=0.13 Motor activity: 152.05 (21.25) vs. 106.51 (21.96) P=0.08 Number of HRV rhythms: 1.98 (0.19) vs. 2.39 (0.19) P=0.07	NR	NR

Note: AD=administrative database, AOR=adjusted odds ratio, ADHD=attention deficit hyperactivity disorder, ASD=atrial septal defects, BMI=body mass index, BRS=Behavioral Rating Scale, CC=case control, CES-D= Center for Epidemiologic Studies Depression Scale, CGI-I=Clinical Global Impression scale - Improvement, CGI-S=Clinical Global Impression Scale - Severity, CI=confidence interval, CNS=central nervous system, CV=cardiovascular, DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, ECG=electrocardiogram, ETOH=alcohol, FDA=US Food and Drug Administration, GA=gestational age, GI=gastrointestinal, GP=general practitioner, HAM-A=Hamilton Anxiety Rating Scale, HAM-D=Hamilton Depression Rating Scale, IQ=intelligence quotient, IQR=Interquartile range, ITT=intention to treat, LD=linked database, LMP=last menstrual period, MADRS=Montgomery-Asberg Depression Rating Scale, MDD=major depressive disorder, mDDD=multiple defined daily dose, MDI=Mental Development Index, MR=mental retardation, MRI=magnetic resonance imaging, NA=not applicable, NBDPS=National Birth Defects Prevention Study, NICU=neonatal intensive care unit, NR=not reported, NSAID=non steroidal anti inflammatory drug, NSD=no significant difference, OCD=obsessive compulsive disorder, OR=odds ratio, PBD=population-based database, PBR=population-based registry, PC=prospective cohort, PDD=pervasive developmental disorder, PDI=Psychomotor Development Index, PPHN=persistent pulmonary hypertension, PTSD=post-traumatic stress disorder, RR=relative risk, RRR=relative risk reduction, SCN=special care nursery, SD=standard deviation, SEIFA= Socio-Economic Indexes for Areas, SES=socio-economic status, SNRI=serotonin norepinephrine reuptake inhibitor, SRI=serotonin reuptake inhibitor, SSRI=selective serotonin reuptake inhibitor, TCA=tricyclic antidepressant, TUS=Teratogen Information Service, UK=United Kingdom, US=United States, VSD=ventricular septal defects.

Evidence Table 2. Risk of Bias Assessment Observational Studies

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Alwan 2007[1] US	Unclear; although patients with pre-gestational diabetes were not pre-specified to be excluded, they were ultimately excluded from the analyses (2.2% cases and 0.5 controls, *P*<0.001)	No, self-report 6 weeks to 2 years after delivery, without validation and no ultrasound to confirm gestational age	Yes	Yes, Yes	Yes
Alwan 2010[2] US	Unclear; consent rates NR; also, although patients with pre-gestational diabetes were not pre-specified to be excluded, they were ultimately excluded from the analyses (2.7% cases and 0.6% controls; *P*<0.001)	No, self-report 6 weeks to 2 years after delivery, without validation and method for confirming gestational age is NR	Yes	Yes, Yes	Yes
Andrade 2009[86]	Yes	Unclear; pharmacy database; length of gestation not available, trimester of exposure based on estimates of gestational age	Yes	Yes	Yes
Bakker 2010 The Netherlands	Unclear; consent rates NR for controls	Unclear; prescription database verified by telephone interview with mother; but methods for confirming gestational age NR	Yes	Unclear, completeness of data NR for controls	Yes
Bakker 2010[4, 5] The Netherlands	Unclear; overall consent rate of 80%, but between-groups comparability NR	Unclear; prescription database verified by telephone interview with mother; but methods for confirming gestational age NR	Yes	Yes, Yes	Yes
Ban 2012[6]	Yes	Unclear	Yes	Yes	Yes
Berard 2007[7]	Yes	Unclear; prescription database, no assessment of compliance; gestational age estimated by LMP	Yes	Unclear; completeness of data NR for controls	Yes
Berle 2004[87]	Unclear, process for selecting control group NR	Yes, serum concentrations	Unclear, not specified	Unclear, NR	Yes
Bogen 2010[8] (companion to Wisner 2009)	Yes	Yes	Yes	No overall=39% Yes differential	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Boucher 2008[9]	Unclear; comparison group from same population-base, but high potential for confounding by indication as comparison is AD exposed or not and depression diagnosis data NR	Unclear; data source is pharmacy database and no methods to overcome uncertainties, few exposure details reported, more concerning in context of narrow exposure window	Unclear, not specified	Yes	Yes
Bracken 1981[88]	Yes	No; self-report without validation (only contacted prescriber in 10% of instances when further info was required)	Yes	Yes overall=13% No for differential: 24% vs 5.5%	No
Casper 2003[10]	Unclear; time frame, number screened, consent rates NR	Unclear; self-report with no validation, but some prospective data and dosages reported	Yes	Unclear; participation rate NR	Yes
Chambers 1996[11] US	Unclear	Unclear (self report, MR corroboration not mentioned)	Yes	Yes	Yes
Chambers 2006[12]	Yes	Unclear; self-report based on structured telephone interview, no validation reported	Yes	Yes	Yes
Chan-Fai-Chan 2005[89] Canada	No - 1) could be a referral bias of some kind causing women to be recommended bupropion may differ by country or database 2) Comparison group was composed from only one of the three data sources	No - self report of exposure by patient with no confirmation	Yes	Unclear	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Cole 2007[13]	Yes	Unclear; prescription database, gestational age estimated by earliest/latest conception	Yes	Unclear; completeness of data not clearly reported, but in Discussion indicates that greater frequency of charts that could not be abstracted in the 'other antidepressant' group	Yes
Cole 2007[14] US	Yes	Unclear - drug dispensing data only	Yes	Yes	Yes
Colvin 2010[90] Australia	Yes	Unclear; first trimester exposure based on LMP	Yes (up to 6 years with definition in citation)	Unclear; missing data for 'general patient' category for 23 medicines with incomplete ascertainment	Yes
Colvin 2011[91] Australia	Unclear - only 80% of the claims data is captured by the PBS database	Unclear - only have drug dispensing data	Yes	Yes	Yes
Colvin 2012[15] Australia	Unclear - only 80% of the claims data is captured by the PBS database	Unclear - only have drug dispensing data	Yes	Yes	Yes
Costei 2002[92] Canada	Unclear; reasons for exclusions NR	No; no verification and no ultrasound.	Yes (presumed though not stated when followup interview performed)	Unclear; completeness of data NR	No (not defined, parental report)

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Croen 2011[16]	Yes	Yes	Unclear; only 18% of autism dx before age 3 this applies to both cases and controls	Unclear; reasons for exclusion of 122 of original 420 cases NR	Yes
Davidson 2009[17] Israel	Unclear (not stated)	Unclear (self-report only? "during entire pregnancy")	Yes	Yes	Yes
Davis 2007[18]	Yes	Unclear; pharmacy database; length of gestation not available, trimester of exposure based on estimates of gestational age	Yes	Overall: 30 days=yes (11%), 365 days=no (42%) Differential: 30 days=unclear, 365 days=yes	Unclear; identified use of ICD-9 codes, but did not pre specify which ones
De Vera 2012[93] Canada	Yes	Yes	Yes	Unclear; completeness of data NR	Yes
Diav-Citrin 2008[94]	Unclear	Unclear	Yes	Unclear	Yes
Djulus 2006[95]	Unclear	Unclear	Yes	Unclear	Yes
Dubnov-Raz 2012[20] Israel	Unclear (not stated)	Unclear (self-report, "any stage")	Yes	Yes	Yes
Dubnov-Raz, 2012[19] Israel	Unclear (control group selected because of murmur and normal echo) Unclear if exposed group identified by self-report	Unclear (method/dose/duration not stated--presumed self-report at onset of labor)	Yes	Yes	Yes
Einarson 2009[96]	Unclear	Unclear	Yes	Unclear	Yes
Einarson 2011[97] Canada	Unclear how group of 1245 exposed women was formed	No (self report)	Yes	Unclear, completeness of data NR	No; definitions NR

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Einarson, 2003[98] Canada	Unclear (only reported number followed)	Unclear (self-report only)	Yes	Unclear (not stated)	Yes
Einarson, 2009[99] Canada	Unclear (not stated)	No; no verification and no ultrasound.	Unclear (timing of followup interview unknown)	Unclear; completeness of data NR	No (no method of assigning malformations reported)
Einarson, 2010[100] Canada	Unclear (report number followed only)	Unclear (self-report only)	Yes	Unclear (not stated)	Yes
El Marroun 2012[21] The Netherlands	Yes	Yes	Yes	Yes	Yes
Ericson 1999[101]	Unclear; population cohort but selection based on drug exposure only	Unclear - not described	Yes	unclear	Yes
Ferreira 2007[22]	Unclear; population cohort but selection based on drug exposure only	Unclear - not described	Yes	Yes	No
Figueroa 2010[23] US	Yes (data set)	No (prescriptions) prescription database without compliance data and gestation estimated by sub tracing 93 days at a time from deliver date	Yes	Unclear	Yes
Gabally 2009[102]	Unclear; very little description	No, appears to be self report without validation	Yes	Yes	Yes
Galbally 2011[103] (companion to Galbally 2009)	Unclear; very little description	No, appears to be self report without validation	Yes	No - 25% overall, 30% in unexposed group and 18.5% in exposed group.	Yes - maternal depression and child development scales
Gorman 2012[24] US	Unclear; 2320 possible; 284 included - not clear how selected. Selection of control group unclear.	No - self report.	Yes	Yes	Yes
Grzeskowiak 2012[25] Australia	Unclear; population cohort but selection based on drug exposure only	Yes	Yes	Unclear	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Hale 2010[104] US	Unclear (who, when, why?)	Unclear (self-report via survey)	Yes	Unclear; completeness of data NR	No (subjective, e.g. "low body temp")
Heikkinen 2002[26] Finland	Unclear (not stated how 11/10 chosen)	Unclear (self report?)	Yes	Yes	Unclear
Jimenez-Solem 2012[27] Denmark	Yes	Unclear - drug dispensing data only	Yes	Yes	Yes
Jimenez-Solem, 2013, Denmark[28]	Yes	Yes	Yes	Yes	Yes
Jordan 2008[29]	Yes	Yes	Yes	Yes	Yes
Kallen 2004[30]	Yes	Unclear; 39% timing not stated	Yes	Yes - see ref number14 for supplemental information	Yes
Kallen 2007[105]	Unclear; population cohort but selection based on drug exposure only	Unclear - exposure primarily self-report.	Yes	Unclear	Yes
Kallen 2007[31] Sweden	Unclear - we don't know if they were depressed or not	No - self-report	Yes	Yes	Yes
Kieler 2012[33] Sweden	Yes	Yes	Yes	Unclear	Yes
Kleiger-Grossmann 2011[106] Canada	Unclear - could be a referral bias of some kind causing women to be recommended escitalopram, may differ by country or database	No - self report of exposure by patient with no confirmation	Unclear - it is unclear if all major malformations (particularly cardiac) would have been detected at the time of followup	No - loss to followup is not reported	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Klinger 2010[107] Israel	Yes	Unclear, self-report without verification	Yes	No (12% with NAS, 55% without)	Yes
Kornum 2010[34] Denmark	Unclear - we don't know if they were depressed or not	Yes	Yes	Yes	Yes
Kulin 1998[108]	Unclear; recruitment time frame not reported, number excluded not reported.	No; self-report without validation, very little detail provided about dose, duration, etc.	Yes	No	No
Laine 2003[35]	Unclear	Unclear - exposed mothers blood was analyzed for drug, but unexposed was not. No other verification methods.	Yes	Yes	Yes
Latendresse, 2011[36] US	Yes	Yes	Unclear	No. 20% excluded after initial enrollment	Yes
Lennestal 2007[37] Sweden	Yes - birth registries	No	Yes (delivery outcomes)	Unclear, completeness of data NR	Yes
Levinson-Castiel 2006[38] Israel	Yes	No, self report with no verification	Yes	Yes	Yes
Lewis 2010[39] Australia	Yes	No - self report only	Yes	Yes	Yes
Logsdon 2011[40] US	Yes	Unclear - drug levels taken only on those thought to be taking SSRs - not everyone.	Yes	Unclear - not reported and it looks like it could be as high as about 30%	Yes
Louik 2007[41] US	Unclear - about 40% of the eligible people refused to participate	No - self-report	Unclear	Yes	Yes
Lund 2009[42] Denmark	Yes	Unclear because self-report and no verification	Yes	Unclear	Yes
Malm 2011[43] Finland	Yes	Yes	Yes	Yes	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Manakova 2011[109] Czech Republic	No. Only describes number followed but not the number eligible for the study.	Unclear	Unclear	Unclear.	No.
Maschi 2008[110] Italy	Yes	No, self report and no validation and unclear about confirmation of gestational age	Yes	Unclear	No.
McElhatton 1996[111] UK	Unclear - unclear that they were including everyone who called.	No - self-report	Yes	No - 16-20% loss to followup	Yes
McFarland 2011[44] US	Yes	No - self-report	Yes	No	Yes
Merlob 2009[45] Israel	Yes	No - self-report	Yes	Yes	Yes
Misri 1991[112] Canada	Unclear; eligibility criteria described, but numbers and reasons for exclusions NR	Unclear, medications managed prospectively, but compliance NR	Yes	Unclear, NR	No
Misri 2006[46] Canada	Unclear: eligibility criteria NR	Unclear, NR	Yes	No (58% attrition in exposed group, 39% in control group)	Yes
Misri 2010[47] Canada	Unclear; eligibility criteria described, but numbers and reasons for exclusions NR	Unclear; methods NR	Yes	Yes overall, 19% loss to followup Unclear differential	Yes
Mulder 2011[48] The Netherlands	Unclear; participation required patient be identified by doctor or midwife and comparability of between-groups consent rates NR	Unclear; self-report	Yes	No; overall high and study group higher than comparison group	Yes
Nakhai-Pour 2010[49] Canada	Yes	Yes	Yes	Yes	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Nijenhuis 2012[113] The Netherlands	Yes Data Base	Unclear; date of conception guessed. Exposure "calculated", unclear compliance. Used admin data base	Yes	Yes	Yes
Nordeng 2012[50] Norway	Yes	Unclear	Yes	Yes	Yes
Nulman 1997[114] Canada	Unclear; exclusions reported, similar consent rates, but inclusion based on self-report and recruitment time frame end date NR	No; self-report without validation, very few exposure details reported	Yes	Yes	No for birth defects and perinatal complications, yes for neurobehavioral
Nulman 2002[83]	Unclear; recruitment time frame end date NR, only reported number followed up	No; self-report without validation, very little detail provided about dose, duration, etc.	Yes	Yes for Reynell, no for Baley (35% missing overall: 18% for fluoxetine group, 39% for TCA group and 505 for comparisons group); no for McCarthy (60% excluded from analysis overall; unclear about differential)	Yes
Nulman 2012[51] Canada	Unclear; although they demonstrated between-group balance in exclusions due to "unable to be located or refused participation", they didn't itemize which groups the 381 who did not meet the inclusion criteria came from	Unclear; self-report	Yes	Yes overall; LTFU higher in TCA group (19% vs 7%)	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Oberlander 2002[52] (2-day), Oberlander 2005[115] (2-month)	Unclear; "consecutive" recruitment, but criteria NR; 63% participation rate overall and between-group comparability in participation rate NR; notes this is part of a larger study, but no citation	Yes	Yes	Yes overall, no differential at 2 days (med=27% vs 12%=controls) and 2 months (17% vs 4%)	Yes
Oberlander 2004[116] Canada	Unclear; exposed cohorts enrolled consecutively, but unclear about controls	Yes, plasma levels	Yes	Yes	Yes
Oberlander 2006[53]	Yes	Unclear; no details about exposure	Yes	Yes	Yes
Oberlander 2007[117] (4-year followup to Oberlander 2005)	Unclear (see Oberlander 2002)	Yes (see Oberlander 2002)	Yes	No for differential (SSRI=52%, control=39%); no for overall=48%	Yes
Oberlander 2008[54]	Unclear; inclusion criteria NR	Yes	Yes	Yes overall (14%); unclear for differential	Yes
Oberlander 2008[55] Canada	Yes	Unclear - drug dispensing data only	Yes	Yes	Yes
Oberlander 2010[118]	Unclear, eligibility criteria NR, described as a convenience sample, no time frame	Unclear, methods NR, but doses reported	Yes	Yes overall (23% after 3 years); between-groups NR	Yes
Okun 2011[56] US	Yes	Yes	Yes	Yes at week 20, no at weeks 30 (27%) and 36 (36%)	Yes
Okun 2012[57] US	Yes	Unclear	Yes	Yes	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Palmsten 2012[58] Canada	Yes	Unclear; gestational age estimated as 280 days prior to estimated delivery date	Yes	Unclear; completeness of data NR	Yes
Pastuszak 1993[119]	Unclear; recruitment time frame NR, only reported number followed up	No; self-report without validation, very few exposure details reported	Yes	Unclear; participation rate NR	No for birth defects, yes for pregnancy outcomes
Pawluski 2009[120] Canada	Unclear; insufficient information	Yes, serum concentrations	Yes	No. 30% missing data (14% in SSRI group vs 50% in non-SSRI group); but no differences between those with and without data	No for neonatal outcomes, yes for neonatal adaptation symptoms and maternal mood
Pearlstein 2006[121] US	Yes	Yes	Unclear; 12 weeks	Overall: No, Differential: No	Unclear
Pearson 2007[59] US	Unclear; only reported number enrolled	Unclear; methods NR	Yes	Yes, no LTFU,	Yes
Pedersen 2009[60] Denmark	Yes	Unclear because database with no compliance data	Yes	Yes: overall, differential: unclear	Yes
Pedersen 2010[61] Denmark	Unclear; comparability of between-groups consent rates NR	Unclear; self-report, no verification	Yes	No for overall: 76% to 79% at 6m and 54% to 62% at 19 months; Yes for differential	Yes
Rai 2013[62] Sweden	Yes	Unclear - relies on self-report	Yes	Yes	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Ramos 2008[84] Canada	Yes	Unclear; pharmacy data; gestational estimated by LMP date, but confirmed between two databases	Yes	Yes for differential; unclear for overall because nonresponders were less likely to be welfare recipients than responders	Yes
Ramos 2010[64] Canada	Yes	Unclear; pharmacy data; gestational estimated by LMP date, but confirmed between two databases	Yes	Yes	Yes
Rampono 2004[122] Australia	Unclear; only reported number enrolled	No; timing is an issue they were taking in 3rd trimester but could have been taking entire pregnancy	Yes	Yes	Yes
Rampono 2009[65] Australia	Unclear; only reported number enrolled	Yes; serum concentrations	Yes	No for overall (25%); unclear for differential	Yes
Reebye 2002[66] British Columbia	Unclear; exposed groups recruited during pregnancy and controls after delivery; unclear how decided who to approach	Unclear; not described, but prospective and dosages reported	Yes	No overall (24%); no differential (17% vs 33%)	Yes
Reis 2010[67] Sweden	Yes	Unclear	Yes	Yes	Yes
Salisbury 2011[68] US	Yes, eligibility criteria described and flow of patient selection described	Yes (TLFB Interview)	Yes - Delivery outcomes, NB assessments	Ratings are No for overall and unclear for differential	Yes
Salkeld 2008[69] Canada	Yes	Yes	Yes	Yes	Yes
Simon 2002[70] US	Yes	Yes	Yes	Yes	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Sit 2011[71] US	Yes	Yes	Yes	No overall (only included 21 of original 48 from 'continuous SSRI exposure group, 44%); unclear differential	Yes
Sivojelezova 2005[123]	Unclear	Unclear	Yes	Unclear	Yes
Stephansson 2013[72] Sweden	Yes	Unclear	Yes	Yes	Yes
Suri 2004[124]	Unclear	Unclear	Yes	Yes	Yes
Suri 2007[73] US	Unclear; numbers and reasons for exclusions NR	Yes	Yes	No overall, 36% excluded from analysis; unclear about differential, NR	Yes
Suri 2011[74] US	Unclear; Higher participation rate in controls (79%) vs Group 1 (67%)	Yes	Yes	Yes	Yes
Toh 2009[125] US/Canada	No (live-born, malformed excluded; since primary outcome GA, pre-term and weight, this may influence)	No (self report, some attempt to verify with bottle, unclear what percent had GA by ultrasound)	Yes	Yes (95% overall, losses not described)	Yes
Toh 2009[75] US/Canada	Yes	No (self report, some attempt to clarify with bottle, LMP and ultrasound as self-report)	Yes	Yes	No (high blood pressure not defined)
Ververs 2009[76] The Netherlands	Yes	Unclear (pharmacy dispensing of "at least one" Rx)	Yes	Yes	Yes
Wen 2006[77] Canada	Yes	Yes	Yes	Unclear, completeness of data NR	Yes

Author Year Country	1. Unbiased patient selection?	2. Adequate exposure ascertainment?	3. Reasonable followup duration?	4. Acceptable levels of differential or overall high loss to followup?	5. Events adequately specified and defined?
Wichman 2009[126] US	Unclear (no info on diagnosis/severity)	Yes	Unclear (similar between groups, but just followed until discharge from birth hospitalization)	Yes	Yes
Wilson 2011[78] US	Unclear (not stated how identified in EMR, controls matched for GA only)	Yes	Yes	Yes	Yes
Wisner 2009[79]/Okun 2012[57] US	Yes	Yes, maternal serum levels	Yes	No overall, 27% missing data (54% delivery data, 46% missing congenital anomaly assessments); unclear differential as between-groups missing data NR	Yes
Wogelius 2006[80] Danish	Yes	Yes	Yes	Yes	Unclear (ICD-9 codes without verification)
Yonkers 2012[81] US	Yes	Unclear (self-report)	Yes	Yes	Yes
Zeskind 2004[82] US	Unclear (how cases and controls were chosen)	Yes	Yes	Yes	Unclear (exact age at which behavioral state monitored not given, just range of all; this is important as infants have very distinct behavior in first hours of life)

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Alwan 2007[1] US	Yes	Yes	Yes	Medium
Alwan 2010[2] US	Yes	Yes	Yes	Medium
Andrade 2009[86]	Unclear; verification of hospital claims with medical charts was only possible in 72% overall; 71% among unexposed and 72% among	Yes	No; matched on age, but data on race, other exposures, meconium aspiration, and NSAID exposure NR; higher rates of diabetes and asthma in exposed group, no control for confounders	Medium
Bakker 2010 The Netherlands	Unclear; ICD-9 or 10 codes, but no information about any verification	Yes	Yes	Medium
Bakker 2010[4, 5] The Netherlands	Yes	Yes	Yes	Medium
Ban 2012[6]	Unclear; use of electronic medical record but no validation	Yes	Yes	Medium
Berard 2007[7]	Unclear; ICD-9 codes, no verification	Yes	Yes	Medium
Berle 2004[87]	Unclear; mothers rated infants using an invalidated symptom score form	Yes	Unclear; stated that groups did not differ with respect to demographic data, but data not shown and no adjustments	High
Bogen 2010[8] (companion to Wisner 2009)	Yes	Yes	Yes	Medium
Boucher 2008[9]	Unclear; blinding, assessor characteristics, accuracy of data collection NR	Yes	Yes	Medium
Bracken 1981[88]	Yes	Yes	No, unable to adjust for covariates because of small numbers	High
Casper 2003[10]	Yes	Yes	Unclear; no adjustment for more miscarriages in unmedicated group (54% vs 29%), but matched on numerous other variables	Medium
Chambers 1996[11] US	Unclear (blinding not stated for all outcomes)	Yes	Yes	Medium
Chambers 2006[12]	Unclear; blinded neonatologist, but pulmonary hypertension documented either by oxygen saturation or echocardiographic evidence and unclear how balanced the methods were between groups	Yes	Yes	Medium
Chan-Fai-Chan 2005[89] Canada	Unclear - assessors were not blinded to group allocation	Yes	Unclear	High
Cole 2007[13]	Yes	Yes	Yes	Medium

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Cole 2007[14] US	Yes	Yes	Unclear - not all confounders were accounted for	Low
Colvin 2010[90] Australia	Unclear (no blinding)	Yes	No (women with Rx may be different)	High
Colvin 2011[91] Australia	Unclear - included only live born infants	Yes	Yes	Medium
Colvin 2012[15] Australia	Unclear - included only live born infants	Yes	Yes	Medium
Costei 2002[92] Canada	No (self-report, no mention of corroboration, no blinding)		Yes (increased smokers in exposure group, but modeling accounted for this)	High
Croen 2011[16]	Yes	Yes	Yes	Medium
Davidson 2009[17] Israel	Unclear (no blinding, SSRI group gets put in incubator; delays in discharge related to this?)	Yes	No (matched for GA only, no controlling)	Medium
Davis 2007[18]	Yes for limb and eye anomalies and spina bifida for which ICD-9 codes were verified by chart review; unclear for others	Yes	Unclear; collected data on age but baseline comparability NR; race and other exposures data not available; parity not mentioned; control for confounders NR	Medium
De Vera 2012[93] Canada	Yes (although no blinding, tightly defined objective variable with cited validation; no increased visits to increase detection)	Yes	Yes	Low
Diav-Citrin 2008[94]	Unclear	Yes	Yes	High
Djulus 2006[95]	Unclear	Yes	Yes	High
Dubnov-Raz 2012[20] Israel	Unclear (blinding?)	Yes	Yes	Medium
Dubnov-Raz, 2012[19] Israel	Yes for ECG outcomes, but other outcomes = unclear	Yes	No (matched for GA only, control group had audible murmur)	Medium
Einarson 2009[96]	Unclear	Yes	Yes	High
Einarson 2011[97] Canada	Unclear; blinding NR, details of corroboration NR	Yes	**Matched for age, smoking, alcohol use, timing of call, but results of matching NR and information based on self-report without verification**	High
Einarson, 2003[98] Canada	Unclear (assume self report, no mention of blinding)	Yes	Unclear (matched, but does not appear to be adjusted for increased smokers in one group)	High
Einarson, 2009[99] Canada	Unclear; no blinding and based on maternal report. Attempts made to corroborate with treating physician, but no information about corroboration rate.	Unclear; individual anomalies NR for the control group NR	Unclear (matched for age, tob, ETOH, but simple stats)	High

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Einarson, 2010[100] Canada	Unclear (asked doctors, but it's not clear how many women gave permission or how many doctors responded)	Yes	Unclear (matched for maternal age, smoking, ETOH only); no group with depression; lack of knowing if ascertainment of the factors matched on was good (self-report)	High
El Marroun 2012[21] The Netherlands	Yes	Yes	Yes	Low
Ericson 1999[101]	Unclear	Yes	No	High
Ferreira 2007[22]	Yes	Yes	Yes	Medium
Figueroa 2010[23] US	Unclear; no validation study of accuracy	Yes	Yes	Medium
Gabally 2009[102]	Birth outcomes - no; depression - yes; withdrawal symptoms – yes	Yes	Unclear	High
Galbally 2011[103] (companion to Galbally 2009)	Birth outcomes - no; depression and child development - yes	Yes	Unclear - control group matched but not stated for what characteristics.	High
Gorman 2012[24] US	Birth outcomes - no (self-report with unclear number confirmed by medical chart); breastfeeding outcomes - yes	Yes	Yes	Medium
Grzeskowiak 2012[25] Australia	Yes	Yes	Yes	Medium
Hale 2010[104] US	No (self report, no blinding)	Unclear (hard to determine which participants are in reporting)	Yes	High
Heikkinen 2002[26] Finland	Unclear (no mention of blinding)	Yes	No (no adjustment)	Medium
Jimenez-Solem 2012[27] Denmark	Unclear - no validation study described	Yes	Yes	Low
Jimenez-Solem, 2013, Denmark[28]	Unclear (methods for verifying the gestational age at death, and also unclear if national records are reliable)	Yes	Yes	Low
Jordan 2008[29]	Unclear - obtained from medical charts where doctor generally knew exposure status	Yes	No	Medium
Kallen 2004[30]	Yes	Yes	Unclear; other than paroxetine they didn't adjust for preterm birth or medical disorders such as diabetes (important for hypoglycemia)	Medium
Kallen 2007[105]	Unclear - ICD-10 code P293B; no validation cited	Yes	Yes	Medium

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Kallen 2007[31] Sweden	Unclear - some data from 2005 is missing, may be screening women/fetuses with ultrasound more in women who take ADs	Yes	Yes	Medium
Kieler 2012[33] Sweden	Unclear - no validation of ICD codes	Yes	Yes	Low
Kleiger-Grossmann 2011[106] Canada	Unclear - assessors were not blinded to group allocation	Yes	Yes	High
Klinger 2010[107] Israel	Yes	Yes	No, higher maternal age in NAS group and this was not controlled for (34 vs 32)	High
Kornum 2010[34] Denmark	No - 1) included only live born infants; 2) accuracy of coding and diagnosis is questioned on p.34; 3) detection bias x 2 sources	Yes	Yes	Medium
Kulin 1998[108]	Yes for major malformations; no for others based on self-report alone	Yes	No; more tobacco use in SSRI group and other differences, no control for differences	High
Laine 2003[35]	Unclear - blinding of outcome assessors intended but stated to not be maintained. Not clear what proportion unblinded.	Yes	No	Medium
Latendresse, 2011[36] US	Unclear. No mention of blinding	Yes	Yes	Medium
Lennestal 2007[37] Sweden	Yes	Yes	Yes	Medium
Levinson-Castiel 2006[38] Israel	Unclear, unblinded assessors	Yes	Unclear, similar in age but no other confounders reported and no regression analysis	Medium
Lewis 2010[39] Australia	Unclear	Yes	No	Medium
Logsdon 2011[40] US	Yes	Yes	No - only race was controlled for	Medium
Louik 2007[41] US	Unclear - not clear how they confirmed specific diagnoses	Yes	Yes	High
Lund 2009[42] Denmark	Unclear, no mention of blinding	Yes	Yes	Medium
Malm 2011[43] Finland	Yes	Yes	Yes	Low
Manakova 2011[109] Czech Republic	No. No mention of blinding	Yes	Unclear	High
Maschi 2008[110] Italy	No	Yes	Yes	High

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
McElhatton 1996[111] UK	Yes	Yes	No - no confounders are adjusted for	High
McFarland 2011[44] US	Yes	Yes	Unclear - they do not adjust for smoking status, comorbidities or other medications	Medium
Merlob 2009[45] Israel	No - cardiologists not blinded to exposure for last 2 years of study	Yes	No - they collected some of them and didn't adjust for them because the sample was too small and there was not matching to the control group	Medium
Misri 1991[112] Canada	Unclear, methods NR	Yes	NA, no between-groups comparison	High
Misri 2006[46] Canada	Yes	Yes	Unclear; similar in age, univariately controlled for depression and anxiety	Medium
Misri 2010[47] Canada	Unclear	Yes	Unclear, only controlled for age and number of children in home	Medium
Mulder 2011[48] The Netherlands	Unclear; blinding NR	Yes	Yes	Medium
Nakhai-Pour 2010[49] Canada	Yes	Yes	Yes	Low
Nijenhuis 2012[113] The Netherlands	Yes	Yes	No, no confounding variables reported or controlled for	High
Nordeng 2012[50] Norway	Yes	Yes	Yes	Medium
Nulman 1997[114] Canada	Yes for neurobehavioral in children (blind psychometrician, standardized instruments); unclear and perinatal complications (verified by pediatrician), but unclear for maternal outcomes	Yes	No; differences in gravidity, parity, previous abortions, SES, alcohol use and cigarette smoking not controlled for	High
Nulman 2002[83]	Yes	Yes	Unclear; multiple linear regression adjusted for differences in maternal depression duration, severity, number episodes, but not number of anxiolytic drugs	Medium for Reynell; High for others
Nulman 2012[51] Canada	Yes	Yes	Unclear; no control for higher gravidity (3 vs 2), previous therapeutic abortions (0.6 vs 0.3), light alcohol use (62% vs 55%) and cigarette smoking (45% vs 31%), lower SES in fluoxetine group (40 vs 46), or genetic factors; assessed based on self-report	High

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Oberlander 2002[52] (2-day), Oberlander 2005[115] (2-month)	Yes	Yes	Unclear; no baseline differences in maternal age or depression, but no other material variables reported.	Medium
Oberlander 2004[116] Canada	Unclear, partial blinding and respiratory symptoms not assessed in a standardized way, only when concern expressed	Yes	Unclear; only age reported and was balanced	High
Oberlander 2006[53]	Yes	Yes	Yes	Medium
Oberlander 2007[117] (4-year followup to Oberlander 2005)	Yes	Yes	Unclear; age was balanced between groups; regression models examined maternal mood, prenatal clonazepam exposure, a history of PNA, and umbilical cord drug levels as predictors of child behavior	High
Oberlander 2008[54]	Yes	Yes; perhaps exception of maternal mood	Unclear; no control for higher levels of depression and anxiety in exposed group.	Medium
Oberlander 2008[55] Canada	Unclear - included only live born infants	Yes	Unclear - key confounders not accounted for	Medium
Oberlander 2010[118]	Unclear; blinding NR	Yes	Unclear; methods for confounding variable ascertainment NR; no adjustment for some baseline differences; non-SSRI exposed group had higher education (18 vs 15 years) and higher rates of 1-10 alcohol drinks (42% vs 24%)	High
Okun 2011[56] US	Unclear, blinding NR	Yes	No, no information about comparability of baseline characteristics between SSRI-exposed and non-exposed groups and no adjustment for confounders	Medium
Okun 2012[57] US	Unclear - they did not use objective tests of sleep latency or have sleep info pre-pregnancy	Yes	Unclear - they note because of the small sample size they were unable to control for all variables	Medium
Palmsten 2012[58] Canada	Unclear-no mention of blinding, wide range of ICD-9 code accuracy in validation study	Yes	Yes	Medium
Pastuszak 1993[119]	Yes, self-report verified by written documentation by pediatrician	Yes	No; age matched, but higher parity in fluoxetine vs NTC and no control	Yes

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Pawluski 2009[120] Canada	Unclear; blinding NR	Yes	Unclear; few characteristics reported, but similar at baseline	High
Pearlstein 2006[121] US	No blinding	Unclear	Unclear if matched for age, race. Baseline characteristics reported overall and not by group.	High
Pearson 2007[59] US	Yes	Yes	Unclear; some differences that were not controlled for: exposed group had lower tobacco use (24% vs 54%) and more married women (97% vs 77%). Also exposed group had higher levels of missing data on tobacco use (40% vs 6%) and marital status (31% vs 10%)	Medium
Pedersen 2009[60] Denmark	No. Only includes live-born infants	Yes	Yes	Medium
Pedersen 2010[61] Denmark	Unclear; self-report, not verification; unblinded assessors	Yes	Unclear; adjusted for multiple factors, but all were measured based on self-report	Medium
Rai 2013[62] Sweden	Yes	Yes	Yes	Low
Ramos 2008[84] Canada	Unclear; ICD-9 codes, no verification	Yes	Yes	Medium
Ramos 2010[64] Canada	Unclear - no data on how reliable database is for this	Yes	Yes; although don't have placental abnormalities or genetic issues which would contribute to both	Medium
Rampono 2004[122] Australia	Unclear; blinding NR	Yes	No; comparability of baseline characteristics NR, no analysis	High
Rampono 2009[65] Australia	Yes	Yes	Unclear; no adjustment for lower proportion of nulliparous (32% vs 56%) and higher proportion of hypertension (21% vs 6%) and alcohol use (24% vs 11%) in case group.	Medium
Reebye 2002[66] British Columbia	Yes	Yes	Unclear; only difference was higher education for control mothers and no adjustment	Medium
Reis 2010[67] Sweden	Yes	Yes	Yes	Medium

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Salisbury 2011[68] US	Yes	Yes	Yes	Medium (due to loss to followup)
Salkeld 2008[69] Canada	Yes	Yes	Yes	Low
Simon 2002[70] US	Unclear - included only live born infants	Yes	Yes	Low
Sit 2011[71] US	Yes	Yes	Unclear; comparability of baseline characteristics NR between fluoxetine and short half-life agents groups, no adjustment	Medium
Sivojelezova 2005[123]	Unclear	Yes	No	High
Stephansson 2013[72] Sweden	Yes	Yes	Yes	Medium
Suri 2004[124]	Unclear	Yes	No	High
Suri 2007[73] US	Yes	Yes	Unclear; no significant differences in age or parity, other important confounders NR	Medium
Suri 2011[74] US	Yes	Yes	Unclear; no significant differences in age or parity, other important confounders NR	Medium
Toh 2009[125] US/Canada	No	Yes	Yes (but confounding by depression could occur)	High
Toh 2009[75] US/Canada	No (self report)	Yes	Yes	Medium
Ververs 2009[76] The Netherlands	Unclear (methods not described for how data obtained or verified)	Yes	No (no adjustment)	Medium
Wen 2006[77] Canada	Unclear. No mention of blinding	Yes	Yes	Medium
Wichman 2009[126] US	Unclear (no mention of blinding)	Yes	No (no adjustment)	High
Wilson 2011[78] US	Unclear (chart review, no blinding)	Yes	Unclear (matched for GA, confounding by depression)	Medium
Wisner 2009[79]/Okun 2012[57] US	Yes	Yes	Yes	Medium
Wogelius 2006[80] Danish	Unclear (no blinding)	Unclear (3 most prevalent)	Yes	Medium

Author Year Country	6. Unbiased and accurate event ascertainment?	7. Free of selective outcome reporting?	8. Adequate handling of potential confounding variables?	Overall Risk of Bias Rating
Yonkers 2012[81] US	Yes	Yes	Yes	Low
Zeskind 2004[82] US	Yes	Yes	Yes	Medium

Note: AD=antidepressant, ETOH=alcohol, GA=gestational age, LMP=last menstrual period, MR=medical record, NA=not applicable, NB=newborn, NR=not reported, NSAID=non steroidal anti inflammatory drug, SES=socio-economic status, SSRI=selective serotonin reuptake inhibitor, TCA=tricyclic antidepressant, UK=United Kingdom, US=United States.

Evidence Table 3. Data Abstraction of Trials

Author Year Country Risk of Bias	Population	Interventions	Age Ethnicity	Other Population Characteristics	Number Randomized
Appleby 1997[127] UK Medium	Inclusion Criteria: Depressed 6-8 weeks after childbirth. Score ≥ 10 on Edinburgh postnatal depression scale; Score ≥ 12 on the revised clinical interview schedule; satisfied research diagnostic criteria for major or minor depressive disorder. Exclusion Criteria: Inadequate English and living outside district. Chronic (>2 years) or resistant depression, current drug or alcohol misuse, severe illness requiring close monitoring or hospital admission, and breast feeding.	1) Fluoxetine + 1 CBT session 2) Fluoxetine + 6 CBT sessions 3) Placebo + 1 CBT session 4) Placebo + 6 CBT sessions Fluoxetine dose NR Time Period: 12 weeks	Mean age: 25 Ethnicity NR	Unplanned Pregnancy: 13.75% Major Depressive Disorder: 12.75% History of Postnatal Depression: 7.5% Family History of postnatal depression: 4%	87
Bloch 2012[128] Israel Medium	Age 18-45 years; criteria met during the screen and baseline visits for current major depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), as assessed by the Structured Clinical Interview for DSM-IV Axis I disorders, and onset of the depressive episode starting within 2 months of parturition.	Three Treatment Groups 1) Sertraline + psychotherapy 2) Placebo + psychotherapy Sertraline mean (SD) dose at 4 weeks: 65.0 (23.5)mg, at 8 weeks: 67.5 (24.5)mg Time Period: 8 wks	Mean age: NR Ethnicity: NR	Anxiety Diagnosis: 22.5% Past Depression: 22.5% Depression in Family: 37.5% Pregnancies: 1.4%	42
Misri, 2004[129] Canada Medium	Age 18-40 years; ≥18 on HAM-D, ≥ 20 on HAM-A and ≥ 12 on EPDS; delivered a healthy baby close to term (37-42 weeks) with a minimum birth weight of 2.5 kg; non smokers; willing to use adequate contraception during the study.	1. Paroxetine 2. Paroxetine + CBT Paroxetine max. dose: 50 mg Time period: 12 weeks	Mean age: 30 White: 62.9% South Asian: 14.3% First Nations: 8.6% Mexican, Spanish, Indo-Canadian, Italian, South-American: 2.8% each	% of children previously born 1: 57% 2: 28.6% 3: 11.4% 4: 2.9% DSM diagnosis Depression only: 2.9% Depression + anxiety: 34.3% Depression + anxiety + obsession: 31.4% Depression+ anxiety + OCD: 31.4%	35

Author Year Country Risk of Bias	Population	Interventions	Age Ethnicity	Other Population Characteristics	Number Randomized
Morrell 2009[130] UK Medium	Inclusion Criteria: At-risk women (who returned a 6-week EPDS score ≥ 12 on the postal questionnaire), had an 8-week EPDS score ≥ 12 when the EPDS was repeated face-to-face by the HV at 8 weeks postnatally. Women eligible for the intervention were therefore defined by two EPDS score ≥ 12. The HV was allowed to provide the intervention to those women whom the HV felt might benefit from the intervention, irrespective of their EPDS score. Women were recruited if they were registered with participating GP practices, became 36 weeks pregnant during the recruitment phase of the trial, had a live baby and were on a collaborating health visitor's caseload for 4 months postnatally.	Primary comparison was between at-risk women randomized to Health Visitor training and women in practices randomized to provide Health Visitor usual care. Six Treatment Groups 1) Cognitive behavioral approach face-to-face 2) Cognitive behavioral approach postal 3) Person-centered approach face-to-face 4) Person-centered approach postal 5) Control (Health Visitor usual care)	Mean age: 30.9 (SD 5.4) Ethnicity: 93.3% White British	93.7% living with others, 6.3% living alone 47.1% first baby	101 clusters in 29 primary care trusts. 595

Author Year Country Trial Name (Quality rating-optional)	Efficacy/effectiveness outcomes	Harms	Funding
Appleby 1997[127] UK Medium	Revised Clinical Interview Schedule Score (Completer Analysis, N=61) % difference in geometric mean scores (95% CI): Fluoxetine vs placebo: 4 weeks=37.1% (5.7% to 58.0%), 12 weeks=40.7% (10.9% to 60.6%); 6 CBT sessions vs 1 CBT session: 4 weeks=53.9% (2.3% to 131.2%), 12 weeks=38.7% (-9.2% to 111.7%) Change in geometric mean scores from baseline to 4 weeks/12 weeks (ITT): Revised Clinical Interview Schedule Fluoxetine+1 CBT session= -16.3/-22.7 Fluoxetine+6 CBT sessions= -16.9/-16.3 Placebo+1 CBT session= -10.4/-10.2 Placebo+6 CBT sessions= -13.7/-14.2 Edinburgh postnatal depression scale Fluoxetine+1 CBT session= -7.1/-9.5 Fluoxetine+6 CBT sessions= -9.7/-10.2 Placebo+1 CBT session= -8.1/-7.2 Placebo+6 CBT sessions= -6.6/6.9 Hamilton score Fluoxetine+1 CBT session= NR/-10 Fluoxetine+6 CBT sessions= NR/-8.9 Placebo+1 CBT session= NR/-5.9 Placebo+6 CBT sessions= NR/-8.9	NR	

Author Year Country Trial Name (Quality rating-optional)	Efficacy/effectiveness outcomes	Harms	Funding
Bloch 2012[128] Israel Medium	Sertraline + psychotherapy vs placebo + psychotherapy Change from baseline at 8 weeks, n=40 (p-values are NS presented as group by time interaction unless otherwise specified for MADRS, EPDS, CGI) Improvement in MADRS -13.86 vs -9.85, significant time effect p<0.0001 Improvement in EPDS: -9.75 vs -3.55, significant time effect p<0.0001 Improvement in CGI-S: -1.9 vs -1.5 Improvement in CGI-I: -2.00 vs -0.25 Response rates at 8 weeks MADRS or EPDS, n=40: 70% vs 55%, p=NS Remission rates at 8 weeks MADRS or EPDS, n=40, 65% vs 50%, p=NS	Hypomaniac switch in 10% of patients in sertraline +psychotherapy group vs 0 in placebo	Independent investigator award for National Alliance on Research on Schizophrenia and Depression
Misri, 2004[128] Canada Medium	Paroxetine vs Paroxetine +CBT Change from baseline (reduction) at final visit (P<0.01 for all) HAM-D: 17.6 vs 15.2 HAM-A: 14.3 vs 14.6 EPDS: 8.4 vs 10.2 YBOCS: 4.9 vs 9.1 CGI-I: 2.75 vs 2.59 % patients with reduction in symptom scores at final visit ≥50% score (p=NS between groups) HAM-D: 87.5 vs 78.9 HAM-A: 75.0 vs 84.2 EPDS: 61.5 vs 58.3 ≥60% score reduction in symptom scores at final visit (p=NS between groups) YBOCS: 80.0 vs 78.6 CGI (1=normal, not at all ill) (p=NS between groups) Depression (based on HAM_D): 75 vs 63.2 Anxiety (based on HAM-A): 75 vs 57.9 Obsessions and/or OCD (based on YBOCS): 80 vs 71.4	NR	Glaxo-SmithKline Canada

Author Year Country Trial Name (Quality rating-optional)	Efficacy/effectiveness outcomes	Harms	Funding
Morrell 2009[130] UK Medium	Intervention vs control Proportion of at-risk women with a 6-month Edinburgh Postnatal Depression Scale score >=12 (Primary Outcome) 33.9% vs 45.6% OR, unadjusted: 0.62 (95% CI 0.40, 0.97); P=0.036 OR, adjusted for 6-week EPDS score: 0.64 (95% CI 0.40, 1.01); P=0.058 OR, adjusted for 6-week EPDS score, lives alone, history of postnatal depression, any life events: 0.60 (95% CI 0.38, 0.95); P=0.028 OR, adjusted for lives alone, history of postnatal depression, any life events: 0.57 (95% CI 0.36, 0.90); P=0.017 6-month outcomes: control vs intervention, adjusted mean difference in scores (95% CI) EPDS: -2.1 (-3.3, -0.9), P=0.001 SF-12 PCS: -1.7 (-3.6, 0.1), P=0.069 SF-12 MCS: 5.2 (2.5, 7.8), P=0.001 SF-6D: 0.03 (0.00, 0.06), P=0.025 CORE-OM well-being: -0.3 (-0.5, -0.2), P=0.001 CORE-OM risk: -0.0 (-0.1, 0.0), P=0.149 CORE-OM symptoms: -0.2 (-0.4, -0.1), P=0.005 CORE-OM functioning: -0.3 (-0.4, -0.1), P=0.001 CORE-OM total score: -0.2 (-0.4, -0.1), P=0.001 State anxiety: -3.9 (-6.6, -1.3), P=0.003 Trait anxiety: -3.7 (-6.1, -1.4), P=0.002 PSI parenting distress: 3.5 (1.3, 5.8), P=0.002 PSI PCDI: 2.1 (0.7, 3.5), P=0.003 PSI difficult child: 2.9 (1.7, 4.2), P=0.001 PSI total stress: 9.3 (137.3, 13.4), P=0.001	NR	Government (UK NHS)

Note: CBT=cognitive behavioral therapy, CI=confidence interval, CGI-I=Clinical Global Impression scale - Improvement, CGI-S=Clinical Global Impression Scale - Severity, CORE-OM= Clinical Outcomes in Routine Evaluation , DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, HAM-A=Hamilton Anxiety Rating Scale, HAM-D=Hamilton Depression Rating Scale, ITT=intention to treat, MADRS= Montgomery-Asberg Depression Rating Scale, NR=not reported, OCD=obsessive compulsive disorder, OR=odds ratio, PCDI=Parent Child Dysfunctional Interaction, PSI=Parenting Stress Index, SD=standard deviation, UK=United Kingdom, US=United States.

Evidence Table 4. Risk of Bias Assessment of Trials

Author Year Country	Randomization Adequate?	Allocation Concealment Adequate?	Groups Similar at Baseline?	Eligibility Criteria Specified?	Outcome Assessors Masked?	Care Provider Masked?
Appleby 1997[127] UK	Yes	Unclear	Placebo+1 session counseling younger	yes	Yes to Drug/No to counseling	Yes to Drug/No to counseling
Bloch 2012[128] Israel	Yes	Unclear	Yes	Yes	Yes	Yes
Misri 2004[129] Canada	Yes	Unclear (no details given)	Yes	Yes	Unclear (Yes at baseline, then for followup: "patient's progress was evaluated by the psychiatrist investigator who administered…)	NA
Morrell 2009[130] UK	Yes	Yes	Yes	Yes	Blinding not possible	Blinding not possible
Sharp 2010[131] UK	Yes	Yes	Yes	Yes	No	No
Wisner 2006[132] US	Yes	Unclear - it says randomized by a sequence generated by SPSS but it is unclear if people can see the whole list and so would know what the next assignment would be. If they knew the next assignment it would potentially introduce bias because they could change the order they enrolled a patient to get them into the group.	No - more non-white women were assigned to the sertraline group and no other baseline variables reported.	Yes	Yes	Unclear
Yonkers 2012[81] US	Yes	Unclear	Yes, mostly except IDS-SR score different between 2 groups, $p<0.05$	Yes	Yes	Yes

Author Year Country	Patient masked?	Intention-to-treat analysis	Maintenance of comparable groups	Acceptable levels of crossovers, adherence, and contamination?	Acceptable levels of overall attrition and between-group differences in attrition?	Overall Risk of Bias Rating
Appleby 1997[127] UK	Yes except counseling	Yes	Yes	Unclear	Overall attrition 30%, acceptable between group differences in attrition	Medium
Bloch 2012[128] Israel	Yes	Yes	Yes	Yes for adherence and crossover, unclear for contamination	Yes	Medium
Misri 2004[129] Canada	No	Yes for all but EPDS	Yes	Unclear for all	Yes	Medium
Morrell 2009[130] UK	Blinding not possible	No, 418/595 included in primary statistical analysis. No imputation of missing data.	Yes	Unclear	Yes	Medium
Sharp 2010[131] UK	No	No, At 18 weeks 206/254 included in analysis (19% excluded)	Unclear	Adherence-No, Contamination: No, Crossover: unclear	At 18 weeks, overall attrition acceptable, between group differences: No>10%	High
Wisner 2006[132] US	Yes	Yes for primary, no for secondary	NA, not comparable at baseline	Unclear for all	No - there was 42% attrition in the sertraline group and 24% percent attrition in the nortriptyline group at 8 weeks. This is both high overall and differential attrition.	High
Yonkers 2012[81] US	Yes	No, 44.3% included in the analysis	Yes	High non adherence: 37% (12 in treatment group, 14 in Placebo), Other: unclear	Overall attrition 56%, acceptable between group differences in attrition	High

Note: NA=not applicable, UK=United Kingdom, US=United States.

Appendix F References

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